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                   resulting in a closer connection to BABS
 NEWS  4  AUG 02   IFIPAT/IFIUDB/IFICDB reloaded with new search and display
                   fields
 NEWS  5  AUG 02   CAplus and CA patent records enhanced with European and Japan
                   Patent Office Classifications
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 NEWS  8  AUG 27   BIOTECHABS/BIOTECHDS: Two new display fields added for legal
                   status data from INPADOC
 NEWS  9  SEP 01   INPADOC: New family current-awareness alert (SDI) available
 NEWS 10  SEP 01   New pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover!
 NEWS 11  SEP 01   New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
 NEWS 12  SEP 14   STN Patent Forum to be held October 13, 2004, in Iselin, NJ
 NEWS 13  SEP 27   STANDARDS will no longer be available on STN
 NEWS 14  SEP 27   SWETSCAN will no longer be available on STN

 NEWS EXPRESS  JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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FILE 'HOME' ENTERED AT 17:00:20 ON 29 SEP 2004

=> file medline, uspatful, dgene, embase, wpids, fsta, jicst, biotechds, biosis,
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                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21
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FILE 'MEDLINE' ENTERED AT 17:01:06 ON 29 SEP 2004

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FILE 'JAPIO' ENTERED AT 17:01:06 ON 29 SEP 2004
COPYRIGHT (C) 2004 Japanese Patent Office (JPO)- JAPIO

=> s Smurf
L1 130 SMURF

=> s l1 and activity
L2 48 L1 AND ACTIVITY

=> s Smurf activity
L3 2 SMURF ACTIVITY

=> s Smad
L4 10848 SMAD

=> d l3 ti abs ibib tot

L3 ANSWER 1 OF 2 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
TI Novel isolated Smurf protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating

cancer and to block osteogenesis, hair growth, tooth formation.

AN 2001-071267 [08] WPIDS

AB WO 200077168 A UPAB: 20011129

NOVELTY - An isolated Smurf1 or Smurf2 protein (I), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid (II) encoding (I);

(2) a vector (III) comprising (II);

(3) a host cell (IV) comprising (III);

(4) production of (I);

(5) a transgenic non-human animal that expresses a human (I);

(6) screening (M) for a modulator of **Smurf activity**, comprising detecting modulation of **Smurf activity** in the presence of a test compound relative to **Smurf activity** in the absence of the test compound;

(7) an antibody (V) that specifically binds to (I);

(8) an oligonucleotide or nucleic acid (VI) that specifically hybridizes to (II) under highly stringent conditions; and

(9) promoting a bone morphogenic protein or transforming growth factor (TGF)- beta activation pathway in a cell, comprising suppressing expression of endogenous Smurf in the cell.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Negative regulator of Smad signal transduction; antagonist of BMP and TGF- beta signaling pathway.

The inhibition of Smad1 by Smurf1 was tested. By over expressing Smad1 and Smad2 together with various dosages of Smurf1 in Xenopus animal caps, the ability of Smurf1 to directly antagonize the mesoderm induction activities of Smad1 and Smad2, was tested. The results showed that expression of Smad1 alone induced ventral mesoderm, as demonstrated by expression of the ventral/posterior mesodermal markers Xhox3 and Xcad1. However, co-expression of Smurf1 and Smad1 blocked induction of these markers at all Smurf1 doses tested, demonstrating that Smurf1 can antagonize Smad1 activity.

USE - Expression of (I) from (III) in a cell is useful for inhibiting a bone morphogenic protein (BMP) or transforming growth factor- beta (TGF beta) activation pathway in a cell (claimed). (I) is useful to block chondrogenesis, osteogenesis, blood differentiation, cartilage formation, neural tube patterning, retinal development, heart induction and morphogenesis, hair growth, tooth formation, gamete formation and a wide variety of tissue and organ formation processes, and hinder the regeneration, growth, maintenance, etc., of bone and other tissues that are dependent on the BMP pathway. (I) is useful for screening for various drugs and/or antibodies that can either enhance the BMP pathway, or inhibit it by antagonizing or mimicking the activity of (I), respectively, and in screening assays for identifying specific ligands of (I). (I) is useful as an immunogen to generate antibodies that are useful to alter the BMP pathway by inhibiting (I) or for diagnostic purposes. (I) is useful for treating a disorder associated with BMP or TGF- beta activation, such as cancer. (I) or inhibitor of (I) can be delivered by a vector to modulate Smads, e.g. to prevent Smurf regulation of Smads where BMP or TGF beta activity is desired, such as in bone regeneration or to study Smurf regulator processes in vivo.

Dwg.0/18

ACCESSION NUMBER:	2001-071267 [08] WPIDS
DOC. NO. CPI:	C2001-019969
TITLE:	Novel isolated Smurf protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation.
DERWENT CLASS:	B04 D16
INVENTOR(S):	THOMSEN, G H; WRANA, J
PATENT ASSIGNEE(S):	(HSCR-N) HSC RES & DEV LP; (UYNY) UNIV NEW YORK STATE RES FOUND
COUNTRY COUNT:	93

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000077168	A2	20001221	(200108)*	EN	106
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000056107	A	20010102	(200121)		
EP 1192174	A2	20020403	(200230)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003502064	W	20030121	(200308)		131
CN 1409722	A	20030409	(200345)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000077168	A2	WO 2000-US16250	20000612
AU 2000056107	A	AU 2000-56107	20000612
EP 1192174	A2	EP 2000-941398	20000612
		WO 2000-US16250	20000612
JP 2003502064	W	WO 2000-US16250	20000612
		JP 2001-504003	20000612
CN 1409722	A	CN 2000-811354	20000612

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000056107	A	Based on	WO 2000077168
EP 1192174	A2	Based on	WO 2000077168
JP 2003502064	W	Based on	WO 2000077168

PRIORITY APPLN. INFO: US 1999-138969P 19990611

L3 ANSWER 2 OF 2 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN

TI Novel isolated Smurf protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation; involving vector plasmid pCMV5-mediated gene transfer for expression in host cell

AN 2001-04474 BIOTECHDS

AB An isolated Smurf1 or Smurf2 protein (I), is claimed. Also claimed are: an isolated nucleic acid (II) encoding (I); a vector comprising (II); a host cell; production of (I); a transgenic non-human animal that expresses a human (I); screening for modulator of **Smurf activity**; an antibody that specifically binds to (I); an oligonucleotide or nucleic acid that specifically hybridizes to (II) under stringent conditions; and promoting a bone morphogenic protein or transforming growth factor (TGF)-beta activation pathway in a cell, comprising suppressing expression of endogenous Smurf in the cell. Expression of (I) from the vector in a cell is useful for inhibiting a bone morphogenic protein or TGF-beta activation pathway in a cell. (I) is useful to block chondrogenesis, osteogenesis, blood differentiation, cartilage formation, etc. (I) is useful for screening for various drugs and/or antibodies that can either enhance the bone morphogenic protein pathway, or inhibit it by antagonizing or mimicking the activity of (I), respectively. (I) is useful for treating a disorder associated with bone morphogenic protein or TGF-beta activation, such as cancer. (106pp)

ACCESSION NUMBER: 2001-04474 BIOTECHDS
TITLE: Novel isolated Smurf protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation;
involving vector plasmid pCMV5-mediated gene transfer for expression in host cell
AUTHOR: Thomsen G H; Wrana J
PATENT ASSIGNEE: Univ.New-York-State-Res.Found.; HSC-Res.Develop.
LOCATION: Toronto, Ontario, Canada.
PATENT INFO: WO 2000077168 21 Dec 2000
APPLICATION INFO: WO 2000-US16250 12 Jun 2000
PRIORITY INFO: US 1999-138969 11 Jun 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-071267 [08]

=> d his

(FILE 'HOME' ENTERED AT 17:00:20 ON 29 SEP 2004)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA, JICST-EPLUS, BIOTECHDS, BIOSIS, HCAPLUS, SCISEARCH, BIOBUSINESS, CEN, CEABA-VTB, JAPIO' ENTERED AT 17:01:06 ON 29 SEP 2004
L1 130 S SMURF
L2 48 S L1 AND ACTIVITY
L3 2 S SMURF ACTIVITY
L4 10848 S SMAD

=> d l2 ti abs ibib tot

L2 ANSWER 1 OF 48 MEDLINE on STN
TI Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.
AB The Runt domain transcription factors (RUNXs) play essential roles in normal development and neoplasias. Genetic analyses of animals and humans have revealed the involvement of RUNX1 in hematopoiesis and leukemia, RUNX2 in osteogenesis and cleidocranial dysplasia, and RUNX3 in the development of T-cells and dorsal root ganglion neurons and in the genesis of gastric cancer. Here we report that RUNX3 is a target of the acetyltransferase **activity** of p300. The p300-dependent acetylation of three lysine residues protects RUNX3 from ubiquitin ligase **Smurf**-mediated degradation. The extent of the acetylation is up-regulated by the transforming growth factor-beta signaling pathway and down-regulated by histone deacetylase activities. Our findings demonstrate that the level of RUNX3 protein is controlled by the competitive acetylation and deacetylation of the three lysine residues, revealing a new mechanism for the posttranslational regulation of RUNX3 expression.
ACCESSION NUMBER: 2004349788 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15138260
TITLE: Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.
AUTHOR: Jin Yun-Hye; Jeon Eun-Joo; Li Qing-Lin; Lee Yong Hee; Choi Joong-Kook; Kim Wun-Jae; Lee Kwang-Youl; Bae Suk-Chul
CORPORATE SOURCE: Department of Biochemistry and Urology, School of Medicine and Institute for Tumor Research, Chungbuk National University, Cheongju 361-763, South Korea.
SOURCE: Journal of biological chemistry, (2004 Jul 9) 279 (28) 29409-17.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040716
Last Updated on STN: 20040825
Entered Medline: 20040824

L2 ANSWER 2 OF 48 MEDLINE on STN
TI Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts.
AB The principal effect of TGF-beta1 on mesenchymal cells is its stimulation of ECM synthesis. Previous reports indicated the significance of the autocrine TGF-beta loop in the pathogenesis of scleroderma. In this study, we focused on Smad7 and Smurfs, principal molecules in the negative regulation of TGF-beta signaling, to further understand the autocrine TGF-beta loop in scleroderma. Scleroderma fibroblasts exhibited increased Smad7 levels compared with normal fibroblasts in vivo and in vitro. Smad7 constitutively formed a complex with the TGF-beta receptors, and the inhibitory effect of Smad7 on the promoter **activity** of human alpha2(I) collagen and 3TP-lux was completely impaired in scleroderma fibroblasts. Furthermore, the protein stability of TGF-beta receptor type I was significantly increased in scleroderma fibroblasts compared with normal fibroblasts. There was no significant difference in Smurf1 and Smurf2 levels between normal and scleroderma fibroblasts, and the transiently overexpressed Smurf1 and/or Smurf2 did not affect TGF-beta receptor type I protein levels in scleroderma fibroblasts. These results indicate that the impaired Smad7-**Smurf**-mediated inhibitory effect on TGF-beta signaling might contribute to maintaining the autocrine TGF-beta loop in scleroderma fibroblasts. To our knowledge, this is the first report of a disturbed negative regulation of TGF-beta signaling in fibrotic disorders.
ACCESSION NUMBER: 2004023363 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14722617
TITLE: Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts.
AUTHOR: Asano Yoshihide; Ihn Hironobu; Yamane Kenichi; Kubo Masahide; Tamaki Kunihiko
CORPORATE SOURCE: Department of Dermatology, Faculty of Medicine, University of Tokyo, Tokyo, Japan.
SOURCE: Journal of clinical investigation, (2004 Jan) 113 (2) 253-64.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20040115
Last Updated on STN: 20040210
Entered Medline: 20040209

L2 ANSWER 3 OF 48 MEDLINE on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AB Smad ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory Smad (I-Smad) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-Smad in inhibiting

BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003328281 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12857866
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR: Murakami Gyo; Watabe Tetsuro; Takaoka Kunio; Miyazono Kohei; Imamura Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo 170-8455, Japan.
SOURCE: Molecular biology of the cell, (2003 Jul) 14 (7) 2809-17. Journal code: 9201390. ISSN: 1059-1524.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20030715
Last Updated on STN: 20040414
Entered Medline: 20040413

L2 ANSWER 4 OF 48 MEDLINE on STN
TI Cell cycle regulatory E3 ubiquitin ligases as anticancer targets.
AB Disregulation of the cell cycle and proliferation play key roles in cellular transformation and tumorigenesis. Such processes are intimately tied to the concentration, localization and **activity** of enzymes, adapters, receptors, and structural proteins in cells. Ubiquitination of these cellular regulatory proteins, governed by specific enzymes in the ubiquitin (Ub) conjugation cascade, has profound effects on their various functions, most commonly through proteasome targeting and degradation. This review will focus on a variety of E3 Ub ligases as potential oncology drug targets, with particular emphasis on the role of these molecules in the regulation of stability, localization, and **activity** of key proteins such as tumor suppressors and oncoproteins. E3 ubiquitin ligases that have established roles in cell cycle and apoptosis, such as the anaphase-promoting complex (APC), the Skp-1-Cul1-F-box class, and the murine double minute 2 (MDM2) protein, in addition to more recently discovered E3 ubiquitin ligases which may be similarly important in tumorigenesis, (e.g. **Smurf** family, CHFR, and Efp), will be discussed. We will present evidence to support E3 ligases as good biological targets in the development of anticancer therapeutics and address challenges in drug discovery for these targets.

ACCESSION NUMBER: 2003024782 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12531181
TITLE: Cell cycle regulatory E3 ubiquitin ligases as anticancer targets.
AUTHOR: Pray Todd R; Parlati Francesco; Huang Jianing; Wong Brian R; Payan Donald G; Bennett Mark K; Issakani Sarkiz Daniel; Molineaux Susan; Demo Susan D
CORPORATE SOURCE: Rigel Pharmaceuticals, Inc., 240 East Grand Avenue, South San Francisco, California 94080, USA.. tpray@rigel.com
SOURCE: Drug resistance updates : reviews and commentaries in antimicrobial and anticancer chemotherapy, (2002 Dec) 5 (6) 249-58. Ref: 80
Journal code: 9815369. ISSN: 1368-7646.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030118
Last Updated on STN: 20030521
Entered Medline: 20030520

L2 ANSWER 5 OF 48 MEDLINE on STN
TI The hydrostatic and hydrodynamic volumes of polyols in aqueous solutions and their sweet taste.
AB The tastes and solution properties of sugar alcohols were studied in an attempt to illuminate the mechanism of sweet taste chemoreception. The **SMURF** method was used to measure tastetime-intensity of aqueous solutions of sugar alcohols and the results were interpreted using the Stevens power function and kinetic parameters. The apparent molar volumes, apparent specific volumes, partial molar volumes, partial specific volumes and intrinsic viscosities of the solutions were studied. Apparent molar volume reflects the size of the molecule in a hydrostatic state whereas intrinsic viscosity gives a measure of the size of the molecules in a hydrodynamic state. Generally the apparent molar volumes of the polyols are 6-13% greater than those of the parent sugars, indicating less interaction with the water structure. Apparent specific volume values can predict taste quality, and the average apparent specific volume for the sugar alcohols studied fits within the central part of the sweet range, i.e. 0.5-0.68 cm3/g, which accords with their ability to elicit a pure sweet taste response. Intensities and persistences of sweetness in the polyols followed the same trend as intrinsic viscosities.
ACCESSION NUMBER: 97292388 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9146905
TITLE: The hydrostatic and hydrodynamic volumes of polyols in aqueous solutions and their sweet taste.
AUTHOR: Lopez Chavez A; Birch G G
CORPORATE SOURCE: Department of Agriculture & Food Technology, ITESM, Queretaro, Mexico.
SOURCE: Chemical senses, (1997 Apr) 22 (2) 149-61.
Journal code: 8217190. ISSN: 0379-864X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19970805
Entered Medline: 19970723

L2 ANSWER 6 OF 48 USPATFULL on STN
TI Secure self-organizing and self-provisioning anomalous event detection systems
AB An approach for providing managed security services is disclosed. A database, within a server or a pre-existing anomalous event detection system, stores a rule set specifying a security policy for a network associated with a customer. An anomalous detection event module is deployed within a premise of the customer and retrieves rule sets from the database. The anomalous detection event module monitors a sub-network of the network based on the rule sets. The anomalous event detection module is further configured to self-organize by examining components of the network and to monitor for anomalous events according to the examined components, and to self-provision by selectively creating another instance of the anomalous detection event module to monitor another sub-network of the network.

ACCESSION NUMBER: 2004:234588 USPATFULL
TITLE: Secure self-organizing and self-provisioning anomalous event detection systems
INVENTOR(S): Hoefelmeyer, Ralph Samuel, Colorado Springs, CO, UNITED STATES
Phillips, Theresa E., Fairfax, VA, UNITED STATES
Wiederin, Shawn Edward, Cedar Rapids, IA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004181664	A1	20040916
APPLICATION INFO.:	US 2003-385229	A1	20030310 (10)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WORLDCOM, INC., Technology Law Department, 1133 19th Street, N.W., Washington, DC, 20036
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Page(s)
LINE COUNT: 889

L2 ANSWER 7 OF 48 USPATFULL on STN
TI Internet privacy protection device
AB The invention consists of a standalone broadband plug and play Internet privacy protection device that provides complete computer or network security for always-on high speed connections by means of combining a real-time packet inspection process in conjunction with computer or network IP address concealment and implementing a seamless network disconnection upon detection of Internet inactivity by the client.

ACCESSION NUMBER: 2004:210555 USPATFULL
TITLE: Internet privacy protection device
INVENTOR(S): Sami, Vikash Krishna, Burnaby, CANADA
Paraskake, Michael, Vancouver, CANADA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004162992	A1	20040819
APPLICATION INFO.:	US 2003-364322	A1	20030219 (10)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Mr. Paul Prade, SAAFNET INTERNATIONAL INC., 5945 Kathleen Avenue, 6th Floor, Burnaby, British Columbia, V5H 4 J7
NUMBER OF CLAIMS: 54
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 1606

L2 ANSWER 8 OF 48 USPATFULL on STN
TI Multilayered intrusion detection system and method
AB A multilayered intrusion detection system and method are disclosed. The method includes monitoring **activity** on a network and maintaining a registry of each host node address associated with a host node operable to perform host-based intrusion detection services. The method further includes comparing a destination address of the monitored network **activity** with at least one host node address in the registry. If an address of the network **activity** matches an address of a registered host node, the network **activity** is dismissed and allowed to proceed unencumbered to the registered host node. The network **activity** not destined for a registered host node has intrusion detection services performed on it. The network **activity** dismissed to the host node has intrusion detection services performed on it at the receiving host node.

ACCESSION NUMBER: 2004:200079 USPATFULL
TITLE: Multilayered intrusion detection system and method
INVENTOR(S): Baker, Stephen M., San Antonio, TX, United States
PATENT ASSIGNEE(S): Cisco Technology, Inc., San Jose, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6775657	B1	20040810	
APPLICATION INFO.:	US 1999-471508		19991222	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Starks, Jr., Wilbert L.
ASSISTANT EXAMINER: Booker, Kelvin
LEGAL REPRESENTATIVE: Baker Botts L.L.P.
NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1085

L2 ANSWER 9 OF 48 USPATFULL on STN
TI Method and apparatus for permitting visualizing network data
AB Methods and apparatuses for the visualization of network traffic and permitting access thereto are provided. In one aspect of the invention, an illustrative method includes defining a plurality of views of network traffic for the classification of network traffic into the views. At least one of the views is a group view. In one example, the types of views include at least two of the following: network address, application, protocol, flow type, packet type, geographic region, ICMP type, slow scan, operating system, flag, remote host count, local host count, spoofing, fragments, service, sessions, response time, status, and user. In another example, network traffic is classified according to the composite views of various combinations of previously defined views. A master console permits users to access only the portion of the network for which the users is responsible. The permitted view does not show other parts of the network.

ACCESSION NUMBER: 2004:185771 USPATFULL
TITLE: Method and apparatus for permitting visualizing network data
INVENTOR(S): Newton, Chris, Douglas, CANADA
Bird, William, Estey's Bridge, CANADA
Spencer, Dwight, Douglas, CANADA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004143658	A1	20040722	
APPLICATION INFO.:	US 2003-346920	A1	20030117	(10)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: James C. Scheller, Jr., BLAKELY, SOKOLOFF, TAYLOR & ZAFMAN LLP, Seventh Floor, 12400 Wilshire Boulevard, Los Angeles, CA, 90025-1026
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 439

L2 ANSWER 10 OF 48 USPATFULL on STN
TI Specification-based anomaly detection
AB A method for network intrusion detection on a network comprising a plurality of state machines for passing a plurality of network packets comprises determining frequency distributions for each transition within

each state machine, determining the distributions of values of each state machine on each transition, and comparing the distributions to observed statistics in the network, and upon determining that the observed statistics are outside defined limits, detecting an anomaly.

ACCESSION NUMBER: 2004:128631 USPATFULL
TITLE: Specification-based anomaly detection
INVENTOR(S): Sekar, Ramasubramanian, East Setauket, NY, UNITED STATES
PATENT ASSIGNEE(S): Research Foundation of the State University of New York (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004098617	A1	20040520
APPLICATION INFO.:	US 2002-298826	A1	20021118 (10)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Frank Chau, F. CHAU & ASSOCIATES, LLP, Suite 501, 1900 Hempstead Turnpike, East Meadow, NY, 11554
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 1033

L2 ANSWER 11 OF 48 USPATFULL on STN
TI Method and system to collect geographic location information for a network address utilizing geographically dispersed data collection agents
AB A method and a system perform geolocation activities relating to a network address. A database of network addresses, and associated geographic locations, is maintained. A query, including a network address, is received against the database for a geographic location associated with the network address. Information, concerning the query received against the database, is logged. Geolocation activities relating to at least the network address are modified based on the logged information.

ACCESSION NUMBER: 2004:102619 USPATFULL
TITLE: Method and system to collect geographic location information for a network address utilizing geographically dispersed data collection agents
INVENTOR(S): Anderson, Mark, Westminster, CO, UNITED STATES
Bansal, Ajay, San Jose, CA, UNITED STATES
Doctor, Brad, Broomfield, CO, UNITED STATES
Hadjiyiannis, George, Boston, MA, UNITED STATES
Herringshaw, Christopher, West Wardsboro, VT, UNITED STATES
Karplus, Eli E., Heidelberg, GERMANY, FEDERAL REPUBLIC OF
Muniz, Derald, Midlothian, TX, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004078490	A1	20040422
APPLICATION INFO.:	US 2003-686135	A1	20031014 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-825675, filed on 3 Apr 2001, GRANTED, Pat. No. US 6684250

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-194761P	20000403 (60)
	US 2000-241776P	20001018 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BLAKELY SOKOLOFF TAYLOR & ZAFMAN, 12400 WILSHIRE BOULEVARD, SEVENTH FLOOR, LOS ANGELES, CA, 90025
NUMBER OF CLAIMS: 48
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 64 Drawing Page(s)
LINE COUNT: 3160

L2 ANSWER 12 OF 48 USPATFULL on STN
TI Method and system to associate a geographic location information with a network address using a combination of automated and manual process
AB A method and a system map a geographic location to a network address. At least one automated process is performed to identify a geographic location for the network address. A determination is made whether the automated process provided satisfactory geographic location information for the network address. If the automated process did not provided satisfactory geographic location information for the network address, then the network address is forwarded for manual resolution.

ACCESSION NUMBER: 2004:102618 USPATFULL
TITLE: Method and system to associate a geographic location information with a network address using a combination of automated and manual process
INVENTOR(S): Anderson, Mark, Westminster, CO, UNITED STATES
Bansal, Ajay, San Jose, CA, UNITED STATES
Doctor, Brad, Broomfield, CO, UNITED STATES
Hadjiyiannis, George, Boston, MA, UNITED STATES
Herringshaw, Christopher, West Wardsboro, VT, UNITED STATES
Karplus, Eli E., Heidelberg, GERMANY, FEDERAL REPUBLIC OF
Muniz, Derald, Midlothian, TX, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004078489	A1	20040422
APPLICATION INFO.:	US 2003-685692	A1	20031014 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-825675, filed on 3 Apr 2001, GRANTED, Pat. No. US 6684250

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-194761P	20000403 (60)
	US 2000-241776P	20001018 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BLAKELY SOKOLOFF TAYLOR & ZAFMAN, 12400 WILSHIRE BOULEVARD, SEVENTH FLOOR, LOS ANGELES, CA, 90025
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 64 Drawing Page(s)
LINE COUNT: 3114

L2 ANSWER 13 OF 48 USPATFULL on STN
TI Method and system to modify geolocation activities based on logged query information
AB A method and a system perform geolocation activities relating to a network address. A database of network addresses, and associated geographic locations, is maintained. A query, including a network address, is received against the database for a geographic location associated with the network address. Information, concerning the query received against the database, is logged. Geolocation activities relating to at least the network address are modified based on the logged information.

ACCESSION NUMBER: 2004:102496 USPATFULL
TITLE: Method and system to modify geolocation activities based on logged query information
INVENTOR(S): Anderson, Mark, Westminister, CO, UNITED STATES
Bansal, Ajay, San Jose, CA, UNITED STATES
Doctor, Brad, Broomfield, CO, UNITED STATES
Hadjiyiannis, George, Boston, MA, UNITED STATES
Herringshaw, Christopher, West Wardsboro, VT, UNITED STATES
Karplus, Eli E., Heidelberg, GERMANY, FEDERAL REPUBLIC OF
Muniz, Derald, Midlothian, TX, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004078367	A1	20040422
APPLICATION INFO.:	US 2003-685991	A1	20031014 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-825675, filed on 3 Apr 2001, GRANTED, Pat. No. US 6684250

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-194761P	20000403 (60)
	US 2000-241776P	20001018 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BLAKELY SOKOLOFF TAYLOR & ZAFMAN, 12400 WILSHIRE BOULEVARD, SEVENTH FLOOR, LOS ANGELES, CA, 90025
NUMBER OF CLAIMS: 54
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 64 Drawing Page(s)
LINE COUNT: 3168

L2 ANSWER 14 OF 48 USPATFULL on STN
TI Method and system to initiate geolocation activities on demand and responsive to receipt of a query
AB A method and the system perform geolocation activities relating to a network address. A query, including a network address, is received from an external entity at a geolocation system. Responsive to receipt of the query, geolocation activities are initiated at the geolocation system to map the network address to a geographic location.

ACCESSION NUMBER: 2004:89604 USPATFULL
TITLE: Method and system to initiate geolocation activities on demand and responsive to receipt of a query
INVENTOR(S): Anderson, Mark, Westminster, CO, UNITED STATES
Bansal, Ajay, San Jose, CA, UNITED STATES
Doctor, Brad, Broomfield, CO, UNITED STATES
Hadjiyiannis, George, Boston, MA, UNITED STATES
Herringshaw, Christopher, West Wardsboro, VT, UNITED STATES
Karplus, Eli E., Heidelberg, GERMANY, FEDERAL REPUBLIC OF
Muniz, Derald, Midlothian, TX, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004068582	A1	20040408
APPLICATION INFO.:	US 2003-686102	A1	20031014 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-825675, filed on 3 Apr 2001, GRANTED, Pat. No. US 6684250

	NUMBER	DATE

PRIORITY INFORMATION:	US 2000-194761P	20000403 (60)
	US 2000-241776P	20001018 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	BLAKELY SOKOLOFF TAYLOR & ZAFMAN, 12400 WILSHIRE BOULEVARD, SEVENTH FLOOR, LOS ANGELES, CA, 90025	
NUMBER OF CLAIMS:	36	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	64 Drawing Page(s)	
LINE COUNT:	3092	

L2 ANSWER 15 OF 48 USPATFULL on STN

TI System and method for detecting and countering a network attack

AB Protecting a host network from a flood-type denial of service attack by performing statistical analysis of data packets in the network. The statistical analysis comprises comparing evaluated items in the data packets to threshold values and detecting the attack when the statistical items exceed the threshold value. A countermeasure can be initiated to protect the host network from the attack.

ACCESSION NUMBER:	2004:71696 USPATFULL		
TITLE:	System and method for detecting and countering a network attack		
INVENTOR(S):	Etheridge, James K., Jupiter, FL, UNITED STATES Anton, Richard N., Jupiter, FL, UNITED STATES		
PATENT ASSIGNEE(S):	Cyber Operations, LLC, Jupiter, FL, UNITED STATES (U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004054925	A1	20040318
APPLICATION INFO.:	US 2002-243631	A1	20020913 (10)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	KING & SPALDING, 191 PEACHTREE STREET, N.E., ATLANTA, GA, 30303-1763		
NUMBER OF CLAIMS:	24		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	12 Drawing Page(s)		
LINE COUNT:	1021		

L2 ANSWER 16 OF 48 USPATFULL on STN

TI Methods and materials for transformation

AB Disclosed herein are novel methods and materials directed to transforming a host cell and expressing exogenous RNA therein. Specifically disclosed are DNA-launching platforms used to introduce a replicating viral segment attached to an exogenous polynucleotide into a cell, whereby the exogenous polynucleotide is expressed in said cell and confers a detectable trait.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2004:59043 USPATFULL		
TITLE:	Methods and materials for transformation		
INVENTOR(S):	Rasochova, Lada, Madison, WI, UNITED STATES German, Thomas, Hollandale, WI, UNITED STATES Ahlquist, Paul, Madison, WI, UNITED STATES		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004045050	A1	20040304
APPLICATION INFO.:	US 2003-609207	A1	20030626 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-316622, filed on 21 May 1999, ABANDONED		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-86526P	19980522 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SALIWANCHIK LLOYD & SALIWANCHIK, A PROFESSIONAL ASSOCIATION, 2421 N.W. 41ST STREET, SUITE A-1, GAINESVILLE, FL, 326066669
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 20 Drawing Page(s)
LINE COUNT: 2817
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 17 OF 48 USPATFULL on STN
TI Method and apparatus for facilitating detection of network intrusion
AB System for facilitating detection of network intrusion. Through continuous accumulation of network traffic parameter information, data for a particular session is reduced to a single metric that represents the threat potential of the session as compared to normal network traffic. An analysis station accumulates and maintains the historical data and defines a point for each specific session within a distribution. The dimensions in the distribution space take into account various network traffic parameters useful in identifying an attack. The distance between a session's point and the centroid of the distribution represents the threat metric. The analysis station can display the threat metric as a point or points on a display. The intensity of the point is an indication of the threat potential. The easy-to-read display calls anomalous traffic to the attention of an operator and facilitates discrimination among ambiguous cases.

ACCESSION NUMBER: 2003:336115 USPATFULL
TITLE: Method and apparatus for facilitating detection of network intrusion
INVENTOR(S): Fretwell, Lyman Jefferson, JR., Randolph, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003236995	A1	20031225
APPLICATION INFO.:	US 2002-177078	A1	20020621 (10)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEVEN B. PHILLIPS, MOORE & VAN ALLEN, 2200 WEST MAIN STREET, SUITE 800, DURHAM, NC, 27705
NUMBER OF CLAIMS: 70
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 19 Drawing Page(s)
LINE COUNT: 1896

L2 ANSWER 18 OF 48 USPATFULL on STN
TI Detecting randomness in computer network traffic
AB A method, system and computer program product for detecting denial-of-service attacks. The randomness in the Internet Protocol (IP) source addresses of transmitted IP packets may be detected by performing a hash function on the IP source addresses thereby generating one or more different hash values. If a high number of different hash values were generated for a small number of IP packets evaluated, then random IP source addresses may be detected. By detecting random source IP addresses, a denial-of-service attack may be detected.

ACCESSION NUMBER: 2003:284096 USPATFULL
TITLE: Detecting randomness in computer network traffic

INVENTOR(S): Jeffries, Clark Debs, Durham, NC, UNITED STATES
Jong, Wuchieh James, Raleigh, NC, UNITED STATES
Randall, Grayson Warren, Cary, NC, UNITED STATES
Vu, Ken Van, Cary, NC, UNITED STATES
PATENT ASSIGNEE(S): International Business Machines Corporation, Armonk, NY, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003200441	A1	20031023
APPLICATION INFO.:	US 2002-127031	A1	20020419 (10)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: IBM CORPORATION, PO BOX 12195, DEPT 9CCA, BLDG 002, RESEARCH TRIANGLE PARK, NC, 27709
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 823

L2 ANSWER 19 OF 48 USPATFULL on STN
TI Novel methods of diagnosis of angiogenesis, compositions and methods of screening for angiogenesis modulators
AB Described herein are methods and compositions that can be used for diagnosis and treatment of angiogenic phenotypes and angiogenesis-associated diseases. Also described herein are methods that can be used to identify modulators of angiogenesis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:219636 USPATFULL
TITLE: Novel methods of diagnosis of angiogenesis, compositions and methods of screening for angiogenesis modulators
INVENTOR(S): Murray, Richard, Cupertino, CA, UNITED STATES
Glynne, Richard, Palo Alto, CA, UNITED STATES
Watson, Susan R., El Cerrito, CA, UNITED STATES
PATENT ASSIGNEE(S): Eos Biotechnology, Inc., South San Francisco, CA, UNITED STATES, 94080 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003152926	A1	20030814
APPLICATION INFO.:	US 2001-21660	A1	20011206 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-784356, filed on 14 Feb 2001, PENDING Continuation-in-part of Ser. No. US 2000-637977, filed on 11 Aug 2000, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-148425P	19990811 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
LINE COUNT: 10887
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 20 OF 48 USPATFULL on STN
TI IMPROVED MATERIALS AND METHODS FOR TRANSFORMATION
AB Disclosed herein are novel methods and materials directed to transforming a host cell and expressing exogenous RNA therein. Specifically disclosed are DNA-launching platforms used to introduce a

replicating viral segment attached to an exogenous polynucleotide into a cell, whereby the exogenous polynucleotide is expressed in said cell and confers a detectable trait.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:107763 USPATFULL			
TITLE:	IMPROVED MATERIALS AND METHODS FOR TRANSFORMATION			
INVENTOR(S):	RASOCHOVA, LADA, MADISON, WI, UNITED STATES GERMAN, THOMAS, HOLLANDALE, WI, UNITED STATES AHLQUIST, PAUL, MADISON, WI, UNITED STATES			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003074677	A1	20030417	
APPLICATION INFO.:	US 1999-316622	A1	19990521	(9)
	NUMBER		DATE	
PRIORITY INFORMATION:	US 1998-86526P		19980522	(60)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	APPLICATION			
LEGAL REPRESENTATIVE:	SALIWANCHIK LLOYD & SALIWANCHIK, A PROFESSIONAL ASSOCIATION, 2421 N.W. 41ST STREET, SUITE A-1, GAINESVILLE, FL, 326066669			
NUMBER OF CLAIMS:	30			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	22 Drawing Page(s)			
LINE COUNT:	2809			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 21 OF 48 USPATFULL on STN

TI Method and apparatus for estimating a geographic location of a networked entity

AB A method and an apparatus operates to associate a geographic location associated with a network address. At least one data collection operation is performed to obtain information pertaining to a network address. The retrieved information is processed to identify a plurality of geographic locations potentially associated with the network address, and to attach a confidence factor to each of the plurality of geographic locations. An estimated geographic location is selected from the plurality of geographic locations as being a best estimate of a true geographic location of the network address, where the selection of the estimated geographic location is based upon a degree of confidence-factor weighted agreement within the plurality of geographic locations.

ACCESSION NUMBER:	2003:107557 USPATFULL			
TITLE:	Method and apparatus for estimating a geographic location of a networked entity			
INVENTOR(S):	Anderson, Mark, Westminster, CO, UNITED STATES Bansal, Ajay, Cupertino, CA, UNITED STATES Doctor, Brad, Broomfield, CO, UNITED STATES Hadjiyiannis, George, Cambridge, MA, UNITED STATES Herringshaw, Christopher, West Wardsboro, VT, UNITED STATES Karplus, Eli E., New Castle, CO, UNITED STATES Muniz, Derald, Midlothian, TX, UNITED STATES			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003074471	A1	20030417	
	US 6684250	B2	20040127	
APPLICATION INFO.:	US 2001-825675	A1	20010403	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-194761P	20000403 (60)
	US 2000-241776P	20001018 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Andre I. Marais, BLAKELY, SOKOLOFF, TAYLOR & ZAFMAN LLP, Seventh Floor, 12400 Wilshire Boulevard, Los Angeles, CA, 90025-1026
NUMBER OF CLAIMS: 135
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 63 Drawing Page(s)
LINE COUNT: 3810

L2 ANSWER 22 OF 48 USPATFULL on STN
TI Network surveillance and security system
AB A system that monitors and protects the security of computer networks uses artificial intelligence, including learning algorithms, neural networks and genetic programming, to learn from security events. The invention maintains a knowledge base of security events that updates autonomously in real time. The invention encrypts communications to exchange changes in its knowledge base with separate security systems protecting other computer networks. The invention autonomously alters its security policies in response to ongoing events. The invention tracks network communication traffic from inception at a well-known port throughout the duration of the communication including monitoring of any port the communication is switched to. The invention is able to track and utilize UNIX processes for monitoring, threat detection, and threat response functions. The invention is able to subdivide the network communications into identifying tags for tracking and control of the communications without incurring lags in response times.

ACCESSION NUMBER: 2003:72739 USPATFULL
TITLE: Network surveillance and security system
INVENTOR(S): Carter, Ernst B., San Francisco, CA, UNITED STATES
Zolotov, Vasily, San Francisco, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003051026	A1	20030313
APPLICATION INFO.:	US 2001-766560	A1	20010119 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: THOMPSON COBURN, LLP, ONE FIRSTAR PLAZA, SUITE 3500, ST LOUIS, MO, 63101
NUMBER OF CLAIMS: 40
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 25 Drawing Page(s)
LINE COUNT: 5642

L2 ANSWER 23 OF 48 USPATFULL on STN
TI Countermeasures for irregularities in financial transactions
AB A system and method for identifying financial transactions with the potential for financial irregularity (e.g. money laundering) comprises processing (20) financial transactions connected with a client, account and financial application, subjecting the client/account and transaction information to a set of rules (22) to produce numerical outcomes (116, 124, 132) indicative of the potential for money laundering being present. A user of the system is able to vary the weightings associated with each rule according to their importance to the particular circumstances of the institution in question.

ACCESSION NUMBER: 2003:45915 USPATFULL
TITLE: Countermeasures for irregularities in financial

transactions
INVENTOR(S): Bosworth-Davies, Rowan, London, UNITED KINGDOM
Norfolk, Robert David, Worcester, UNITED KINGDOM
Burd, Paul, Tyler's Green, UNITED KINGDOM

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003033228	A1	20030213
APPLICATION INFO.:	US 2001-998360	A1	20011129 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 2000-29229	20001130

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: UNISYS Corporation, Unisys Way, MS/E8-114, Blue Bell, PA, 19424-0001
NUMBER OF CLAIMS: 65
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Page(s)
LINE COUNT: 1104

L2 ANSWER 24 OF 48 USPATFULL on STN
TI Scripted distributed denial-of-service (DDoS) attack discrimination using turing tests
AB A system, method and computer program product can include a test performed by a computer to determine whether a requestor of resources is a human user or a computer software scripted agent. If the test is passed, then the computer of the present invention assumes that the requestor of resources is a valid human user and access to resources is granted. In an exemplary embodiment of the present invention a system, method and computer program product for controlling access to resources. In an exemplary embodiment the method can include the steps of receiving a request from an entity; presenting the entity with a test; determining from the test whether or not the entity is an intelligent being; and granting the request only if the entity is determined to be an intelligent being.

ACCESSION NUMBER: 2002:222702 USPATFULL
TITLE: Scripted distributed denial-of-service (DDoS) attack discrimination using turing tests
INVENTOR(S): Tyree, David Spencer, Reston, VA, UNITED STATES
PATENT ASSIGNEE(S): NETWORKS ASSOCIATES TECHNOLOGY, INC. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002120853	A1	20020829
APPLICATION INFO.:	US 2001-793733	A1	20010227 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Edward A. Pennington Esq., SWIDLER BERLIN SHEREFF FRIEDMAN, LLP, 3000 K Street, Suite 300, Washington, DC, 20007
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 969

L2 ANSWER 25 OF 48 USPATFULL on STN
TI Method and system for detecting unusual events and application thereof in computer intrusion detection
AB An automated decision engine is utilized to screen incoming alarms using a knowledge-base of decision rules. The decision rules are updated with the assistance of a data mining engine that analyzes historical data.

"Normal" alarm events, sequences, or patterns generated by sensors under conditions not associated with unusual occurrences (such as intrusion attacks) are characterized and these characterizations are used to contrast normal conditions from abnormal conditions. By identifying frequent occurrences and characterizing them as "normal" it is possible to easily identify anomalies which would indicate a probable improper occurrence. This provides very accurate screening capability based on actual event data.

ACCESSION NUMBER: 2002:158272 USPATFULL
TITLE: Method and system for detecting unusual events and application thereof in computer intrusion detection
INVENTOR(S): Manganaris, Stefanos, Durham, NC, UNITED STATES
Hermiz, Keith, Arlington, VA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002082886	A1	20020627
APPLICATION INFO.:	US 2000-749095	A1	20001227 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-230486P	20000906 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Mark D. Simpson, Esquire, Synnestvedt & Lechner LLP, 2600 Aramark Tower, 1101 Market Street, Philadelphia, PA, 19107-2950
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 623

L2 ANSWER 26 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Transforming growth factor-β stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.
AB The Runt domain transcription factors (RUNXs) play essential roles in normal development and neoplasias. Genetic analyses of animals and humans have revealed the involvement of RUNX1 in hematopoiesis and leukemia, RUNX2 in osteogenesis and cleidocranial dysplasia, and RUNX3 in the development of T-cells and dorsal root ganglion neurons and in the genesis of gastric cancer. Here we report that RUNX3 is a target of the acetyltransferase **activity** of p300. The p300-dependent acetylation of three lysine residues protects RUNX3 from ubiquitin ligase **Smurf**-mediated degradation. The extent of the acetylation is up-regulated by the transforming growth factor-β signaling pathway and down-regulated by histone deacetylase activities. Our findings demonstrate that the level of RUNX3 protein is controlled by the competitive acetylation and deacetylation of the three lysine residues, revealing a new mechanism for the posttranslational regulation of RUNX3 expression.
ACCESSION NUMBER: 2004300181 EMBASE
TITLE: Transforming growth factor-β stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.
AUTHOR: Jin Y.-H.; Jeon E.-J.; Li Q.-L.; Lee Y.H.; Choi J.-K.; Kim W.-J.; Lee K.-Y.; Bae S.-C.
CORPORATE SOURCE: K.-Y. Lee, Department of Biochemistry, Sch. of Med. and Inst. for Tum. Res., Chungbuk National University, Cheongju 361-763, Korea, Republic of. ginsenoside@runx3.co.kr
SOURCE: Journal of Biological Chemistry, (9 Jul 2004) 279/28 (29409-29417).
Refs: 38

ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L2 ANSWER 27 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

TI Germline stem cell number in the Drosophila ovary is regulated by redundant mechanisms that control Dpp signaling.

AB The available experimental data support the hypothesis that the cap cells (CpCs) at the anterior tip of the germarium form an environmental niche for germline stem cells (GSCs) of the Drosophila ovary. Each GSC undergoes an asymmetric self-renewal division that gives rise to both a GSC, which remains associated with the CpCs, and a more posterior located cystoblast (CB). The CB upregulates expression of the novel gene, bag of marbles (bam), which is necessary for germline differentiation. Decapentaplegic (Dpp), a BMP2/4 homologue, has been postulated to act as a highly localized niche signal that maintains a GSC fate solely by repressing bam transcription. Here, we further examine the role of Dpp in GSC maintenance. In contrast to the above model, we find that an enhancer trap inserted near the Dpp target gene, Daughters against Dpp (Dad), is expressed in additional somatic cells within the germarium, suggesting that Dpp protein may be distributed throughout the anterior germarium. However, Dad-lacZ expression within the germline is present only in GSCs and to a lower level in CBs, suggesting there are mechanisms that actively restrict Dpp signaling in germ cells. We demonstrate that one function of Bam is to block Dpp signaling downstream of Dpp receptor activation, thus establishing the existence of a negative feedback loop between the action of the two genes. Moreover, in females doubly mutant for bam and the ubiquitin protein ligase **Smurf**, the number of germ cells responsive to Dpp is greatly increased relative to the number observed in either single mutant. These data indicate that there are multiple, genetically redundant mechanisms that act within the germline to downregulate Dpp signaling in the Cb and its descendants, and raise the possibility that a Cb and its descendants must become refractory to Dpp signaling in order for germline differentiation to occur.

ACCESSION NUMBER: 2004237954 EMBASE
TITLE: Germline stem cell number in the Drosophila ovary is regulated by redundant mechanisms that control Dpp signaling.
AUTHOR: Casanueva M.O.; Ferguson E.L.
CORPORATE SOURCE: E.L. Ferguson, Committee on Developmental Biology, University of Chicago, Chicago, IL 60637, United States. elfergus@midway.uchicago.edu
SOURCE: Development, (2004) 131/9 (1881-1890).
Refs: 36
ISSN: 0950-1991 CODEN: DEVPED
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 021 Developmental Biology and Teratology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L2 ANSWER 28 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

TI Impaired Smad7-**Smurf**-mediated negative regulation of TGF-β signaling in scleroderma fibroblasts.

AB The principal effect of TGF-β on mesenchymal cells is its stimulation of ECM synthesis. Previous reports indicated the significance of the autocrine TGF-β loop in the pathogenesis of scleroderma. In this study, we focused on Smad7 and Smurfs, principal molecules in the negative

regulation of TGF-β signaling, to further understand the autocrine TGF-β loop in scleroderma. Scleroderma fibroblasts exhibited increased Smad7 levels compared with normal fibroblasts in vivo and in vitro. Smad7 constitutively formed a complex with the TGF-β receptors, and the inhibitory effect of Smad7 on the promoter **activity** of human α2(1) collagen and 3TP-lux was completely impaired in scleroderma fibroblasts. Furthermore, the protein stability of TGF-β receptor type I was significantly increased in scleroderma fibroblasts compared with normal fibroblasts. There was no significant difference in Smurf1 and Smurf2 levels between normal and scleroderma fibroblasts, and the transiently overexpressed Smurf1 and/or Smurf2 did not affect TGF-β receptor type I protein levels in scleroderma fibroblasts. These results indicate that the impaired Smad7-**Smurf** -mediated inhibitory effect on TGF-β signaling might contribute to maintaining the autocrine TGF-β loop in scleroderma fibroblasts. To our knowledge, this is the first report of a disturbed negative regulation of TGF-β signaling in fibrotic disorders.

ACCESSION NUMBER: 2004190200 EMBASE
TITLE: Impaired Smad7-**Smurf**-mediated negative regulation of TGF-β signaling in scleroderma fibroblasts.
AUTHOR: Asano Y.; Ihn H.; Yamane K.; Kubo M.; Tamaki K.
CORPORATE SOURCE: H. Ihn, Department of Dermatology, Faculty of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. 1N-DER@h.u-tokyo.ac.jp
SOURCE: Journal of Clinical Investigation, (2004) 113/2 (253-264). Refs: 37
ISSN: 0021-9738 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 013 Dermatology and Venereology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

L2 ANSWER 29 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AB Smad ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-β type I receptor through the inhibitory Smad (I-Smad) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-Smad in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003293267 EMBASE
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR: Murakami G.; Watabe T.; Takaoka K.; Miyazono K.; Imamura T.
CORPORATE SOURCE: K. Miyazono, Department of Biochemistry, Cancer Inst. Japan. Found. Cancer R., Tokyo 170-8455, Japan. miyazono-ind@umin.ac.jp
SOURCE: Molecular Biology of the Cell, (1 Jul 2003) 14/7 (2809-2817). Refs: 29

ISSN: 1059-1524 CODEN: MBCEEV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L2 ANSWER 30 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Cell cycle regulatory E3 ubiquitin ligases as anticancer targets.
AB Disregulation of the cell cycle and proliferation play key roles in cellular transformation and tumorigenesis. Such processes are intimately tied to the concentration, localization and **activity** of enzymes, adapters, receptors, and structural proteins in cells. Ubiquitination of these cellular regulatory proteins, governed by specific enzymes in the ubiquitin (Ub) conjugation cascade, has profound effects on their various functions, most commonly through proteasome targeting and degradation. This review will focus on a variety of E3 Ub ligases as potential oncology drug targets, with particular emphasis on the role of these molecules in the regulation of stability, localization, and **activity** of key proteins such as tumor suppressors and oncoproteins. E3 ubiquitin ligases that have established roles in cell cycle and apoptosis, such as the anaphase-promoting complex (APC), the Skp-1-Cu11-F-box class, and the murine double minute 2 (MDM2) protein, in addition to more recently discovered E3 ubiquitin ligases which may be similarly important in tumorigenesis, (e.g. **Smurf** family, CHFR, and Efp), will be discussed. We will present evidence to support E3 ligases as good biological targets in the development of anticancer therapeutics and address challenges in drug discovery for these targets. .COPYRGT. 2002 Elsevier Science Ltd. All rights reserved.
ACCESSION NUMBER: 2003048760 EMBASE
TITLE: Cell cycle regulatory E3 ubiquitin ligases as anticancer targets.
AUTHOR: Pray T.R.; Parlati F.; Huang J.; Wong B.R.; Payan D.G.; Bennett M.K.; Issakani S.D.; Molineaux S.; Demo S.D.
CORPORATE SOURCE: S.D. Demo, Rigel Pharmaceuticals, Inc., 240 East Grand Avenue, South San Francisco, CA 94080, United States. sdemo@rigel.com
SOURCE: Drug Resistance Updates, (2002) 5/6 (249-258).
Refs: 81
ISSN: 1368-7646 CODEN: DRUPFW
PUBLISHER IDENT.: S 1368-7646(02)00121-8
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

L2 ANSWER 31 OF 48 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
TI Identifying protein-protein interactions, useful e.g. in drug development, comprises introducing into cells one or more prey proteins labeled with an epitope tag and one or more bait proteins labeled with a detectable substance.
AN 2004-315601 [29] WPIDS
AB WO2004023146 A UPAB: 20040505
NOVELTY - Identifying protein-protein interactions comprising prey proteins interacting with one or more bait comprises introducing one or more prey proteins in labeled with an epitope tag and one or more bait protein in cells labeled with a detectable substance.
DETAILED DESCRIPTION - Identifying protein-protein interactions comprising prey proteins interacting with one or more bait comprises:
(a) introducing one or more prey proteins in cells, where a prey is labeled with an epitope tag permitting separation of the prey protein from

other proteins in the cells;

(b) introducing one or more bait protein in cells, where a bait protein is labeled with a detectable substance permitting detection of the bait protein and protein-protein interactions comprising a prey protein and the bait protein;

(c) inducing formation of protein-protein interactions between a prey and bait protein; and

(d) assaying for protein-protein interactions comprising a prey protein and bait protein by detecting the detectable substance.

INDEPENDENT CLAIMS are also included for:

(1) quantitating protein-protein interactions;

(2) determining an interactome for one or more bait protein;

(3) determining the functions of gene product;

(4) systematically and quantitatively analyzing protein-protein interactions in cell signaling;

(5) determining the changes in an interactome of mitotic kinase during cell cycle progression;

(6) analyzing protein-protein interactions in different cell types;

(7) assaying for changes in protein-protein interactions in response to intracellular and extracellular factors;

(8) identifying a potential modulator of signal transduction **activity**; and

(9) an agent, modulator or inhibitor identified by a method of (8).

ACTIVITY - Antiinflammatory; Cytostatic.

No biological data given.

MECHANISM OF ACTION - None Given.

USE - The method and kits are useful in identifying, quantifying and analyzing protein-protein interactions. The method is useful in determining a disease or condition associated with a test protein, monitoring the course of therapy, conducting a drug discovery business and in detecting mutations in cellular proteins. The pharmaceutical composition is useful in treating and preventing a disease or condition associated with an abnormality in a signal transduction pathway, e.g. fibrosis, inflammation or cancer.

Dwg.0/3

ACCESSION NUMBER: 2004-315601 [29] WPIDS
DOC. NO. NON-CPI: N2004-251489
DOC. NO. CPI: C2004-119632
TITLE: Identifying protein-protein interactions, useful e.g. in drug development, comprises introducing into cells one or more prey proteins labeled with an epitope tag and one or more bait proteins labeled with a detectable substance.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BARRIOS-RODILES, M; WRANA, J
PATENT ASSIGNEE(S): (MOUN) MOUNT SINAI HOSPITAL
COUNTRY COUNT: 105
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004023146	A2	20040318	(200429)*	EN	53

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

AU 2003264211	A1	20040329	(200459)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 2004023146	A2	WO 2003-CA1354	20030905
AU 2003264211	A1	AU 2003-264211	20030905

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003264211	A1 Based on	WO 2004023146

PRIORITY APPLN. INFO: US 2002-408922P 20020906

L2 ANSWER 32 OF 48 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN

TI Novel isolated **Smurf** protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation.

AN 2001-071267 [08] WPIDS

AB WO 200077168 A UPAB: 20011129

NOVELTY - An isolated Smurf1 or Smurf2 protein (I), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid (II) encoding (I);

(2) a vector (III) comprising (II);

(3) a host cell (IV) comprising (III);

(4) production of (I);

(5) a transgenic non-human animal that expresses a human (I);

(6) screening (M) for a modulator of **Smurf activity**, comprising detecting modulation of **Smurf activity** in the presence of a test compound relative to **Smurf activity** in the absence of the test compound;

(7) an antibody (V) that specifically binds to (I);

(8) an oligonucleotide or nucleic acid (VI) that specifically hybridizes to (II) under highly stringent conditions; and

(9) promoting a bone morphogenic protein or transforming growth factor (TGF)- beta activation pathway in a cell, comprising suppressing expression of endogenous **Smurf** in the cell.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Negative regulator of Smad signal transduction; antagonist of BMP and TGF- beta signaling pathway.

The inhibition of Smad1 by Smurf1 was tested. By over expressing Smad1 and Smad2 together with various dosages of Smurf1 in Xenopus animal caps, the ability of Smurf1 to directly antagonize the mesoderm induction activities of Smad1 and Smad2, was tested. The results showed that expression of Smad1 alone induced ventral mesoderm, as demonstrated by expression of the ventral/posterior mesodermal markers Xhox3 and Xcad1. However, co-expression of Smurf1 and Smad1 blocked induction of these markers at all Smurf1 doses tested, demonstrating that Smurf1 can antagonize Smad1 **activity**.

USE - Expression of (I) from (III) in a cell is useful for inhibiting a bone morphogenic protein (BMP) or transforming growth factor- beta (TGF beta) activation pathway in a cell (claimed). (I) is useful to block chondrogenesis, osteogenesis, blood differentiation, cartilage formation, neural tube patterning, retinal development, heart induction and morphogenesis, hair growth, tooth formation, gamete formation and a wide variety of tissue and organ formation processes, and hinder the regeneration, growth, maintenance, etc., of bone and other tissues that are dependent on the BMP pathway. (I) is useful for screening for various drugs and/or antibodies that can either enhance the BMP pathway, or inhibit it by antagonizing or mimicking the **activity** of (I), respectively, and in screening assays for identifying specific ligands of (I). (I) is useful as an immunogen to generate antibodies that are useful to alter the BMP pathway by inhibiting (I) or for diagnostic purposes. (I) is useful for treating a disorder associated with BMP or TGF- beta activation, such as cancer. (I) or inhibitor of (I) can be delivered by a vector to modulate Smads, e.g. to prevent **Smurf** regulation of

Smads where BMP or TGF beta **activity** is desired, such as in bone regeneration or to study **Smurf** regulator processes in vivo.
Dwg.0/18

ACCESSION NUMBER: 2001-071267 [08] WPIDS
DOC. NO. CPI: C2001-019969
TITLE: Novel isolated **Smurf** protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation.
DERWENT CLASS: B04 D16
INVENTOR(S): THOMSEN, G H; WRANA, J
PATENT ASSIGNEE(S): (HSCR-N) HSC RES & DEV LP; (UYNY) UNIV NEW YORK STATE RES FOUND
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000077168	A2	20001221	(200108)*	EN	106
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000056107	A	20010102	(200121)		
EP 1192174	A2	20020403	(200230)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003502064	W	20030121	(200308)		131
CN 1409722	A	20030409	(200345)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000077168	A2	WO 2000-US16250	20000612
AU 2000056107	A	AU 2000-56107	20000612
EP 1192174	A2	EP 2000-941398	20000612
		WO 2000-US16250	20000612
JP 2003502064	W	WO 2000-US16250	20000612
		JP 2001-504003	20000612
CN 1409722	A	CN 2000-811354	20000612

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000056107	A	Based on	WO 2000077168
EP 1192174	A2	Based on	WO 2000077168
JP 2003502064	W	Based on	WO 2000077168

PRIORITY APPLN. INFO: US 1999-138969P 19990611

L2 ANSWER 33 OF 48 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
TI Novel isolated **Smurf** protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation; involving vector plasmid pCMV5-mediated gene transfer for expression in host cell
AN 2001-04474 BIOTECHDS
AB An isolated Smurf1 or Smurf2 protein (I), is claimed. Also claimed are: an isolated nucleic acid (II) encoding (I); a vector comprising (II); a host cell; production of (I); a transgenic non-human animal that

expresses a human (I); screening for modulator of **Smurf** **activity**; an antibody that specifically binds to (I); an oligonucleotide or nucleic acid that specifically hybridizes to (II) under stringent conditions; and promoting a bone morphogenic protein or transforming growth factor (TGF)-beta activation pathway in a cell, comprising suppressing expression of endogenous **Smurf** in the cell. Expression of (I) from the vector in a cell is useful for inhibiting a bone morphogenic protein or TGF-beta activation pathway in a cell. (I) is useful to block chondrogenesis, osteogenesis, blood differentiation, cartilage formation, etc. (I) is useful for screening for various drugs and/or antibodies that can either enhance the bone morphogenic protein pathway, or inhibit it by antagonizing or mimicking the **activity** of (I), respectively. (I) is useful for treating a disorder associated with bone morphogenic protein or TGF-beta activation, such as cancer. (106pp)

ACCESSION NUMBER: 2001-04474 BIOTECHDS
TITLE: Novel isolated **Smurf** protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation; involving vector plasmid pCMV5-mediated gene transfer for expression in host cell
AUTHOR: Thomsen G H; Wrana J
PATENT ASSIGNEE: Univ.New-York-State-Res.Found.; HSC-Res.Develop.
LOCATION: Toronto, Ontario, Canada.
PATENT INFO: WO 2000077168 21 Dec 2000
APPLICATION INFO: WO 2000-US16250 12 Jun 2000
PRIORITY INFO: US 1999-138969 11 Jun 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2001-071267 [08]

L2 ANSWER 34 OF 48 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.
AB The Runt domain transcription factors (RUNXs) play essential roles in normal development and neoplasias. Genetic analyses of animals and humans have revealed the involvement of RUNX1 in hematopoiesis and leukemia, RUNX2 in osteogenesis and cleidocranial dysplasia, and RUNX3 in the development of T-cells and dorsal root ganglion neurons and in the genesis of gastric cancer. Here we report that RUNX3 is a target of the acetyltransferase **activity** of p300. The p300-dependent acetylation of three lysine residues protects RUNX3 from ubiquitin ligase **Smurf**-mediated degradation. The extent of the acetylation is up-regulated by the transforming growth factor-beta signaling pathway and down-regulated by histone deacetylase activities. Our findings demonstrate that the level of RUNX3 protein is controlled by the competitive acetylation and deacetylation of the three lysine residues, revealing a new mechanism for the posttranslational regulation of RUNX3 expression.

ACCESSION NUMBER: 2004:347664 BIOSIS
DOCUMENT NUMBER: PREV200400349524
TITLE: Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.
AUTHOR(S): Jin, Yun-Hye; Jeon, Eun-Joo; Lin, Qing-; Lee, Yong Hee; Choi, Joong-Kook; Kim, Wun-Jae; Lee, Kwang-Youl [Reprint Author]; Bae, Suk-Chul
CORPORATE SOURCE: Sch MedDept Biochem, Chungbuk Natl Univ, Cheongju, 361763, South Korea
ginsenoside@runx3.co.kr; scbae@med.chungbuk.ac.kr
SOURCE: Journal of Biological Chemistry, (July 9 2004) Vol. 279, No. 28, pp. 29409-29417. print.

CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Aug 2004
Last Updated on STN: 18 Aug 2004

L2 ANSWER 35 OF 48 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts.
AB The principal effect of TGF-beta1 on mesenchymal cells is its stimulation of ECM synthesis. Previous reports indicated the significance of the autocrine TGF-beta loop in the pathogenesis of scleroderma. In this study, we focused on Smad7 and Smurfs, principal molecules in the negative regulation of TGF-beta signaling, to further understand the autocrine TGF-beta loop in scleroderma. Scleroderma fibroblasts exhibited increased Smad7 levels compared with normal fibroblasts in vivo and in vitro. Smad7 constitutively formed a complex with the TGF-beta receptors, and the inhibitory effect of Smad7 on the promoter **activity** of human alpha2(I) collagen and 3TP-lux was completely impaired in scleroderma fibroblasts. Furthermore, the protein stability of TGF-beta receptor type I was significantly increased in scleroderma fibroblasts compared with normal fibroblasts. There was no significant difference in Smurf1 and Smurf2 levels between normal and scleroderma fibroblasts, and the transiently overexpressed Smurf1 and/or Smurf2 did not affect TGF-beta receptor type I protein levels in scleroderma fibroblasts. These results indicate that the impaired Smad7-**Smurf**-mediated inhibitory effect on TGF-beta signaling might contribute to maintaining the autocrine TGF-beta loop in scleroderma fibroblasts. To our knowledge, this is the first report of a disturbed negative regulation of TGF-beta signaling in fibrotic disorders.
ACCESSION NUMBER: 2004:94938 BIOSIS
DOCUMENT NUMBER: PREV200400084043
TITLE: Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts.
AUTHOR(S): Asano, Yoshihide; Ihn, Hironobu [Reprint Author]; Yamane, Kenichi; Kubo, Masahide; Tamaki, Kunihiko
CORPORATE SOURCE: Department of Dermatology, Faculty of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-8655, Japan
IN-DER@h.u-tokyo.ac.jp
SOURCE: Journal of Clinical Investigation, (January 2004) Vol. 113, No. 2, pp. 253-264. print.
CODEN: JCINAO. ISSN: 0021-9738.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Feb 2004
Last Updated on STN: 11 Feb 2004

L2 ANSWER 36 OF 48 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AB Smad ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory Smad (I-Smad) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-Smad in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced

ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003:356072 BIOSIS
DOCUMENT NUMBER: PREV200300356072
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR(S): Murakami, Gyo; Watabe, Tetsuro; Takaoka, Kunio; Miyazono, Kohei [Reprint Author]; Imamura, Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo, 170-8455, Japan
miyazono-ind@umin.ac.jp
SOURCE: Molecular Biology of the Cell, (July 2003) Vol. 14, No. 7, pp. 2809-2817. print.
ISSN: 1059-1524 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 6 Aug 2003

L2 ANSWER 37 OF 48 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Specificity and complexity in **Smurf**-mediated Smad degradation.
ACCESSION NUMBER: 2002:133151 BIOSIS
DOCUMENT NUMBER: PREV200200133151
TITLE: Specificity and complexity in **Smurf**-mediated Smad degradation.
AUTHOR(S): Liang, Min [Reprint author]; Lin, Xia [Reprint author]; Liang, Yao-Yun [Reprint author]; Feng, Xin-Hua [Reprint author]; DeBakey, Michael E. [Reprint author]
CORPORATE SOURCE: Department of Surgery, Baylor College of Medicine, One Baylor Plaza, 139D, Houston, TX, 77030, USA
SOURCE: Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. Supplement, pp. 148a. print.
Meeting Info.: 41st Annual Meeting of the American Society for Cell Biology. Washington DC, USA. December 08-12, 2001. American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Feb 2002
Last Updated on STN: 26 Feb 2002

L2 ANSWER 38 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
TI Transforming Growth Factor-β Stimulates p300-dependent RUNX3 Acetylation, Which Inhibits Ubiquitination-mediated Degradation
AB The Runt domain transcription factors (RUNXs) play essential roles in normal development and neoplasias. Genetic analyses of animals and humans have revealed the involvement of RUNX1 in hematopoiesis and leukemia, RUNX2 in osteogenesis and cleidocranial dysplasia, and RUNX3 in the development of T-cells and dorsal root ganglion neurons and in the genesis of gastric cancer. Here we report that RUNX3 is a target of the acetyltransferase **activity** of p300. The p300-dependent acetylation of three lysine residues protects RUNX3 from ubiquitin ligase **Smurf**-mediated degradation The extent of the acetylation is up-regulated by the transforming growth factor-β signaling pathway and down-regulated by histone deacetylase activities. Our findings demonstrate that the level of RUNX3 protein is controlled by the competitive acetylation and deacetylation of the three lysine residues, revealing a new mechanism for the posttranslational regulation of RUNX3 expression.

ACCESSION NUMBER: 2004:544572 HCAPLUS
DOCUMENT NUMBER: 141:86726
TITLE: Transforming Growth Factor-β Stimulates p300-dependent RUNX3 Acetylation, Which Inhibits Ubiquitination-mediated Degradation
AUTHOR(S): Jin, Yun-Hye; Jeon, Eun-Joo; Li, Qing-Lin; Lee, Yong Hee; Choi, Joong-Kook; Kim, Wun-Jae; Lee, Kwang-Youl; Bae, Suk-Chul
CORPORATE SOURCE: Departments of Biochemistry, School of Medicine and Institute for Tumor Research, Chungbuk National University, Cheongju, 361-763, S. Korea
SOURCE: Journal of Biological Chemistry (2004), 279(28), 29409-29417
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 39 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
TI Impaired Smad7-**Smurf**-mediated negative regulation of TGF-β signaling in scleroderma fibroblasts
AB The principal effect of TGF-β1 on mesenchymal cells is its stimulation of ECM synthesis. Previous reports indicated the significance of the autocrine TGF-β loop in the pathogenesis of scleroderma. In this study, the authors focused on Smad7 and Smurfs, principal mols. in the neg. regulation of TGF-β signaling, to further understand the autocrine TGF-β loop in scleroderma. Scleroderma fibroblasts exhibited increased Smad7 levels compared with normal fibroblasts in vivo and in vitro. Smad7 constitutively formed a complex with the TGF-β receptors, and the inhibitory effect of Smad7 on the promoter **activity** of human α2(I) collagen and 3TP-lux was completely impaired in scleroderma fibroblasts. Furthermore, the protein stability of TGF-β receptor type I was significantly increased in scleroderma fibroblasts compared with normal fibroblasts. There was no significant difference in Smurf1 and Smurf2 levels between normal and scleroderma fibroblasts, and the transiently overexpressed Smurf1 and/or Smurf2 did not affect TGF-β receptor type I protein levels in scleroderma fibroblasts. These results indicate that the impaired Smad7-**Smurf** -mediated inhibitory effect on TGF-β signaling might contribute to maintaining the autocrine TGF-β loop in scleroderma fibroblasts. To our knowledge, this is the first report of a disturbed neg. regulation of TGF-β signaling in fibrotic disorders.
ACCESSION NUMBER: 2004:64890 HCAPLUS
DOCUMENT NUMBER: 140:216014
TITLE: Impaired Smad7-**Smurf**-mediated negative regulation of TGF-β signaling in scleroderma fibroblasts
AUTHOR(S): Asano, Yoshihide; Ihn, Hironobu; Yamane, Kenichi; Kubo, Masahide; Tamaki, Kunihiko
CORPORATE SOURCE: Department of Dermatology, Faculty of Medicine, University of Tokyo, Tokyo, Japan
SOURCE: Journal of Clinical Investigation (2004), 113(2), 253-264
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 40 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN

TI Use of human RING finger protein 11 (RNF11 or PARK8) gene for diagnosis and treatment of late-onset idiopathic Parkinson's disease

AB The present invention provides human RING finger protein 11 gene (PARK8 gene or protein) for diagnosis and treatment of late-onset idiopathic Parkinson's disease. Polymorphisms associated in RNF 11 gene associated with increased susceptibility for Parkinson's disease are provided. Assays for screening for agents that alter the **activity** of a Parkinson's disease polypeptide (PARK8 or RNF11) or which identify PARK8 binding agents for therapy of Parkinson' s disease are disclosed.

ACCESSION NUMBER: 2003:737929 HCAPLUS
DOCUMENT NUMBER: 139:256363
TITLE: Use of human RING finger protein 11 (RNF11 or PARK8) gene for diagnosis and treatment of late-onset idiopathic Parkinson's disease
INVENTOR(S): Hicks, Andrew A.
PATENT ASSIGNEE(S): Decode Genetics Ehf., Iceland
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076658	A2	20030918	WO 2002-IB4276	20021014
WO 2003076658	A3	20031231		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-363220P P 20020308

L2 ANSWER 41 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN

TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads

AB Smad ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation In addition, Smurf1 assocs. with transforming growth factor-β type I receptor through the inhibitory Smad (I-Smad) Smad7 and induces their degradation Herein, we examined whether Smurf1 neg. regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-Smad in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003:571354 HCAPLUS
DOCUMENT NUMBER: 139:302479
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AUTHOR(S): Murakami, Gyo; Watabe, Tetsuro; Takaoka, Kunio; Miyazono, Kohei; Imamura, Takeshi

CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo, 170-8455, Japan
SOURCE: Molecular Biology of the Cell (2003), 14(7), 2809-2817
CODEN: MBCEEV; ISSN: 1059-1524
PUBLISHER: American Society for Cell Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 42 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
TI Cell cycle regulatory E3 ubiquitin ligases as anticancer targets
AB A review. Disregulation of the cell cycle and proliferation play key roles in cellular transformation and tumorigenesis. Such processes are intimately tied to the concentration, localization and **activity** of enzymes, adapters, receptors, and structural proteins in cells. Ubiquitination of these cellular regulatory proteins, governed by specific enzymes in the ubiquitin (Ub) conjugation cascade, has profound effects on their various functions, most commonly through proteasome targeting and degradation This review will focus on a variety of E3 Ub ligases as potential oncol. drug targets, with particular emphasis on the role of these mols. in the regulation of stability, localization, and **activity** of key proteins such as tumor suppressors and oncoproteins. E3 ubiquitin ligases that have established roles in cell cycle and apoptosis, such as the anaphase-promoting complex (APC), the Skp-1-Cull-F-box class, and the murine double minute 2 (MDM2) protein, in addition to more recently discovered E3 ubiquitin ligases which may be similarly important in tumorigenesis, (e.g. **Smurf** family, CHFR, and Efp), will be discussed. We will present evidence to support E3 ligases as good biol. targets in the development of anticancer therapeutics and address challenges in drug discovery for these targets.
ACCESSION NUMBER: 2003:130277 HCAPLUS
DOCUMENT NUMBER: 139:223432
TITLE: Cell cycle regulatory E3 ubiquitin ligases as anticancer targets
AUTHOR(S): Pray, Todd R.; Parlati, Francesco; Huang, Jianing; Wong, Brian R.; Payan, Donald G.; Bennett, Mark K.; Issakani, Sarkiz Daniel; Molineaux, Susan; Demo, Susan D.
CORPORATE SOURCE: Rigel Pharmaceuticals, Inc., South San Francisco, CA, 94080, USA
SOURCE: Drug Resistance Updates (2003), Volume Date 2002, 5(6), 249-258
CODEN: DRUPFW; ISSN: 1368-7646
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 43 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
TI sequences human ubiquitin-protein synthetases as antagonists of BMP and TGF<b signaling pathways and expression during development and interactions with Smad proteins
AB This invention provides unique members of the Hect family of ubiquitin ligases that specifically target BMP and TGF<b/activin pathway-specific Smads. The novel ligases have been named Smurf1 and Smurf2. A transgenic expression system is described for these two proteins. They directly interact with Smads1 and 5 and Smad7, resp., and regulate the ubiquitination, turnover and **activity** of Smads and other proteins of these pathways. Smurf1 interferes with biol. responses to BMP, but not activin signaling. In amphibian embryos Smurf1 inhibits endogenous BMP signals, resulting in altered pattern formation and cell

fate specification in the mesoderm and ectoderm. The present invention provides a unique regulatory link between the ubiquitination pathway and the control of cell fate determination by the TGF<b superfamily during embryonic development. Thus, Smurf1 is a neg. regulator of Smad1 signal transduction, by targeting Smad1, Smurf1 blocks BMP signaling. Screening assays which survey **Smurf** WW domain interaction with Smad protein PPXY domain are also relayed. In mammalian cells, Smurf2 suppresses TGF<b signaling, and in Xenopus, blocks formation of dorsal mesoderm and causes anterior truncation of the embryos. Smurf2 forms a stable complex with Smad7, which induces degradation and downregulation of TGF<b/activin signaling. The human Smurf1 gene was mapped to 7q21.1-q31.1.

ACCESSION NUMBER: 2000:900772 HCAPLUS
DOCUMENT NUMBER: 134:53133
TITLE: sequences human ubiquitin-protein synthetases as antagonists of BMP and TGF<b signaling pathways and expression during development and interactions with Smad proteins
INVENTOR(S): Thomsen, Gerald H.; Wrana, Jeffrey
PATENT ASSIGNEE(S): Research Foundation of State University of New York, USA; HSC Research and Development Limited Partnership
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077168	A2	20001221	WO 2000-US16250	20000612
WO 2000077168	A3	20010503		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000056107	A5	20010102	AU 2000-56107	20000612
EP 1192174	A2	20020403	EP 2000-941398	20000612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:		
US 1999-138969P	P	19990611
WO 2000-US16250	W	20000612

L2 ANSWER 44 OF 48 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

TI Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation

AB The Runt domain transcription factors (RUNXs) play essential roles in normal development and neoplasias. Genetic analyses of animals and humans have revealed the involvement of RUNX1 in hematopoiesis and leukemia, RUNX2 in osteogenesis and cleidocranial dysplasia, and RUNX3 in the development of T-cells and dorsal root ganglion neurons and in the genesis of gastric cancer. Here we report that RUNX3 is a target of the acetyltransferase **activity** of p300. The p300-dependent acetylation of three lysine residues protects RUNX3 from ubiquitin ligase **Smurf**-mediated degradation. The extent of the acetylation is up-regulated by the transforming growth factor-beta signaling pathway and down-regulated by histone deacetylase activities. Our findings demonstrate

that the level of RUNX3 protein is controlled by the competitive acetylation and deacetylation of the three lysine residues, revealing a new mechanism for the posttranslational regulation of RUNX3 expression.

ACCESSION NUMBER: 2004:623078 SCISEARCH
THE GENUINE ARTICLE: 834XX
TITLE: Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation
AUTHOR: Jin Y H; Jeon E J; Li Q L; Lee Y H; Choi J K; Kim W J; Lee K Y (Reprint); Bae S C
CORPORATE SOURCE: Chungbuk Natl Univ, Sch Med, Dept Biochem, Cheongju 361763, South Korea (Reprint); Chungbuk Natl Univ, Sch Med, Dept Urol, Cheongju 361763, South Korea; Chungbuk Natl Univ, Inst Tumor Res, Cheongju 361763, South Korea
COUNTRY OF AUTHOR: South Korea
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (9 JUL 2004) Vol. 279, No. 28, pp. 29409-29417.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 38
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L2 ANSWER 45 OF 48 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts
AB The principal effect of TGF-beta1 on mesenchymal cells is its stimulation of ECM synthesis. Previous reports indicated the significance of the autocrine TGF-beta loop in the pathogenesis of scleroderma. In this study, we focused on Smad7 and Smurfs, principal molecules in the negative regulation of TGF-beta signaling, to further understand the autocrine TGF-beta loop in scleroderma. Scleroderma Fibroblasts exhibited increased Smad7 levels compared with normal fibroblasts in vivo and in vitro. Smad7 constitutively formed a complex with the TGF-beta receptors, and the inhibitory effect of Smad7 on the promoter **activity** of human alpha2(I) collagen and 3TP-lux was completely impaired in scleroderma fibroblasts. Furthermore, the protein stability of TGF-beta receptor type I was significantly increased in scleroderma fibroblasts compared with normal fibroblasts. There was no significant difference in Smurf1 and Smurf2 levels between normal and scleroderma fibroblasts, and the transiently overexpressed Smurf1 and/or Smurf2 did not affect TGF-beta receptor type I protein levels in scleroderma fibroblasts. These results indicate that the impaired Smad7-**Smurf**-mediated inhibitory effect on TGF-beta signaling might contribute to maintaining the autocrine TGF-beta loop in scleroderma fibroblasts. To our knowledge, this is the first report of a disturbed negative regulation of TGF-beta signaling in fibrotic disorders.

ACCESSION NUMBER: 2004:103644 SCISEARCH
THE GENUINE ARTICLE: 764EZ
TITLE: Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts
AUTHOR: Asano Y; Ihn H (Reprint); Yamane K; Kubo M; Tamaki K
CORPORATE SOURCE: Univ Tokyo, Fac Med, Dept Dermatol, Bunkyo Ku, 7-3-1 Hongo, Tokyo 1138655, Japan (Reprint); Univ Tokyo, Fac Med, Dept Dermatol, Bunkyo Ku, Tokyo 1138655, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (JAN 2004) Vol. 113, No. 2, pp. 253-264.
Publisher: AMER SOC CLINICAL INVESTIGATION INC, 35 RESEARCH DR, STE 300, ANN ARBOR, MI 48103 USA.

ISSN: 0021-9738.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 37
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L2 ANSWER 46 OF 48 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AB Smad ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory Smad (I-Smad) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-Smad in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.
ACCESSION NUMBER: 2003:636252 SCISEARCH
THE GENUINE ARTICLE: 701CB
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AUTHOR: Murakami G; Watabe T; Takaoka K; Miyazono K (Reprint); Imamura T
CORPORATE SOURCE: Japanese Fdn Canc Res, Inst Canc, Dept Biochem, Tokyo 1708455, Japan (Reprint); Shinshu Univ, Dept Orthoped Surg, Nagano 3908621, Japan; Univ Tokyo, Dept Mol Pathol, Grad Sch Med, Tokyo 1130033, Japan; Osaka City Univ, Sch Med, Dept Orthoped Surg, Osaka 5458585, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (JUL 2003) Vol. 14, No. 7, pp. 2809-2817.
Publisher: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD 20814-2755 USA.
ISSN: 1059-1524.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 29
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L2 ANSWER 47 OF 48 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Cell cycle regulatory E3 ubiquitin ligases as anticancer targets
AB Disregulation of the cell cycle and proliferation play key roles in cellular transformation and tumorigenesis. Such processes are intimately tied to the concentration, localization and **activity** of enzymes, adapters, receptors, and structural proteins in cells. Ubiquitination of these cellular regulatory proteins, governed by specific enzymes in the ubiquitin (Ub) conjugation cascade, has profound effects on their various functions, most commonly through proteasome targeting and degradation. This review will focus on a variety of E3 Ub ligases as potential oncology drug targets, with particular emphasis on the role of these molecules in the regulation of stability, localization, and **activity** of key proteins such as tumor suppressors and oncoproteins. E3 ubiquitin ligases that have established roles in cell cycle and apoptosis, such as the anaphase-promoting complex (APC), the Skp-1-Cul1-F-box class, and the

murine double minute 2 (MDM2) protein, in addition to more recently discovered E3 ubiquitin ligases which may be similarly important in tumorigenesis, (e.g. **Smurf** family, CHFR, and Efp), will be discussed. We will present evidence to support E3 ligases as good biological targets in the development of anticancer therapeutics and address challenges in drug discovery for these targets.

ACCESSION NUMBER: 2003:132808 SCISEARCH
THE GENUINE ARTICLE: 639NT
TITLE: Cell cycle regulatory E3 ubiquitin ligases as anticancer targets
AUTHOR: Pray T R; Parlati F; Huang J N; Wong B R; Payan D G; Bennett M K; Issakani S D; Molineaux S; Demo S D (Reprint)
CORPORATE SOURCE: Rigel Pharmaceut Inc, 240 E Grand Ave, San Francisco, CA 94080 USA (Reprint); Rigel Pharmaceut Inc, San Francisco, CA 94080 USA
COUNTRY OF AUTHOR: USA
SOURCE: DRUG RESISTANCE UPDATES, (DEC 2002) Vol. 5, No. 6, pp. 249-258.
Publisher: CHURCHILL LIVINGSTONE, JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND.
ISSN: 1368-7646.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 81
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L2 ANSWER 48 OF 48 SCISEARCH on STN
TI The DSmurf ubiquitin-protein ligase restricts BMP signaling spatially and temporally during Drosophila embryogenesis
AB We identified Drosophila **Smurf** (DSmurf) as a negative regulator of signaling by the BMP2/4 ortholog DPP during embryonic dorsal-ventral patterning. DSmurf encodes a HECT domain ubiquitin-protein ligase, homologous to vertebrate Smurf1 and Smurf2, that binds the Smad1/5 ortholog MAD and likely promotes its proteolysis. The essential function of DSmurf is restricted to its action on the DPP pathway. DSmurf has two distinct, possibly mechanistically separate, functions in controlling DPP signaling. Prior to gastrulation, DSmurf mutations cause a spatial increase in the DPP gradient, as evidenced by ventrolateral expansion in expression domains of target genes representing all known signaling thresholds. After gastrulation, DSmurf mutations cause a temporal delay in downregulation of earlier DPP signals, resulting in a lethal defect in hindgut organogenesis.
ACCESSION NUMBER: 2002:375865 SCISEARCH
THE GENUINE ARTICLE: 546XK
TITLE: The DSmurf ubiquitin-protein ligase restricts BMP signaling spatially and temporally during Drosophila embryogenesis
AUTHOR: Podos S D; Hanson K K; Wang Y C; Ferguson E L (Reprint)
CORPORATE SOURCE: Univ Chicago, Dept Mol Genet & Cell Biol, Chicago, IL 60637 USA (Reprint); Univ Chicago, Dept Organismal Biol & Anat, Chicago, IL 60637 USA
COUNTRY OF AUTHOR: USA
SOURCE: DEVELOPMENTAL CELL, (OCT 2001) Vol. 1, No. 4, pp. 567-578.
Publisher: CELL PRESS, 1100 MASSACHUSETTES AVE,, CAMBRIDGE, MA 02138 USA.
ISSN: 1534-5807.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 55
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

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=> d his

     (FILE 'HOME' ENTERED AT 17:00:20 ON 29 SEP 2004)

     FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA, JICST-EPLUS,
     BIOTECHDS, BIOSIS, HCAPLUS, SCISEARCH, BIOBUSINESS, CEN, CEABA-VTB,
     JAPIO' ENTERED AT 17:01:06 ON 29 SEP 2004
L1           130 S SMURF
L2            48 S L1 AND ACTIVITY
L3             2 S SMURF ACTIVITY
L4         10848 S SMAD

=> s l2 and l4
L5           12 L2 AND L4

=> s l4 and ubiquitination
L6          219 L4 AND UBIQUITINATION

=> s l5 and l6
L7            8 L5 AND L6

=> d l7 ti abs ibib tot

L7   ANSWER 1 OF 8     MEDLINE on STN
TI   Transforming growth factor-beta stimulates p300-dependent RUNX3
     acetylation, which inhibits ubiquitination-mediated degradation.
AB   The Runt domain transcription factors (RUNXs) play essential roles in
     normal development and neoplasias. Genetic analyses of animals and humans
     have revealed the involvement of RUNX1 in hematopoiesis and leukemia,
     RUNX2 in osteogenesis and cleidocranial dysplasia, and RUNX3 in the
     development of T-cells and dorsal root ganglion neurons and in the genesis
     of gastric cancer. Here we report that RUNX3 is a target of the
     acetyltransferase activity of p300. The p300-dependent
     acetylation of three lysine residues protects RUNX3 from ubiquitin ligase
     Smurf-mediated degradation. The extent of the acetylation is
     up-regulated by the transforming growth factor-beta signaling pathway and
     down-regulated by histone deacetylase activities. Our findings
     demonstrate that the level of RUNX3 protein is controlled by the
     competitive acetylation and deacetylation of the three lysine residues,
     revealing a new mechanism for the posttranslational regulation of RUNX3
     expression.
ACCESSION NUMBER:    2004349788     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 15138260
TITLE:               Transforming growth factor-beta stimulates p300-dependent
                     RUNX3 acetylation, which inhibits ubiquitination
                     -mediated degradation.
AUTHOR:              Jin Yun-Hye; Jeon Eun-Joo; Li Qing-Lin; Lee Yong Hee; Choi
                     Joong-Kook; Kim Wun-Jae; Lee Kwang-Youl; Bae Suk-Chul
CORPORATE SOURCE:    Department of Biochemistry and Urology, School of Medicine
                     and Institute for Tumor Research, Chungbuk National
                     University, Cheongju 361-763, South Korea.
SOURCE:              Journal of biological chemistry, (2004 Jul 9) 279 (28)
                     29409-17.
                     Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200408
ENTRY DATE:          Entered STN: 20040716
                     Last Updated on STN: 20040825
                     Entered Medline: 20040824
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L7 ANSWER 2 OF 8 MEDLINE on STN

TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.

AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced **ubiquitination** and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their **ubiquitination** and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003328281 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12857866
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR: Murakami Gyo; Watabe Tetsuro; Takaoka Kunio; Miyazono Kohei; Imamura Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo 170-8455, Japan.
SOURCE: Molecular biology of the cell, (2003 Jul) 14 (7) 2809-17. Journal code: 9201390. ISSN: 1059-1524.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20030715
Last Updated on STN: 20040414
Entered Medline: 20040413

L7 ANSWER 3 OF 8 EMBASE on STN

TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.

AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-β type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced **ubiquitination** and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their **ubiquitination** and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003293267 EMBASE
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.

AUTHOR: Murakami G.; Watabe T.; Takaoka K.; Miyazono K.; Imamura T.
CORPORATE SOURCE: K. Miyazono, Department of Biochemistry, Cancer Inst. Japan. Found. Cancer R., Tokyo 170-8455, Japan. miyazono-ind@umin.ac.jp
SOURCE: Molecular Biology of the Cell, (1 Jul 2003) 14/7 (2809-2817).
Refs: 29
ISSN: 1059-1524 CODEN: MBCEEV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L7 ANSWER 4 OF 8 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
TI Novel isolated **Smurf** protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation.
AN 2001-071267 [08] WPIDS
AB WO 200077168 A UPAB: 20011129
NOVELTY - An isolated Smurf1 or Smurf2 protein (I), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an isolated nucleic acid (II) encoding (I);
(2) a vector (III) comprising (II);
(3) a host cell (IV) comprising (III);
(4) production of (I);
(5) a transgenic non-human animal that expresses a human (I);
(6) screening (M) for a modulator of **Smurf activity**, comprising detecting modulation of **Smurf activity** in the presence of a test compound relative to **Smurf activity** in the absence of the test compound;
(7) an antibody (V) that specifically binds to (I);
(8) an oligonucleotide or nucleic acid (VI) that specifically hybridizes to (II) under highly stringent conditions; and
(9) promoting a bone morphogenic protein or transforming growth factor (TGF)- beta activation pathway in a cell, comprising suppressing expression of endogenous **Smurf** in the cell.
ACTIVITY - Cytostatic.
MECHANISM OF ACTION - Negative regulator of **Smad** signal transduction; antagonist of BMP and TGF- beta signaling pathway.
The inhibition of Smad1 by Smurf1 was tested. By over expressing Smad1 and Smad2 together with various dosages of Smurf1 in Xenopus animal caps, the ability of Smurf1 to directly antagonize the mesoderm induction activities of Smad1 and Smad2, was tested. The results showed that expression of Smad1 alone induced ventral mesoderm, as demonstrated by expression of the ventral/posterior mesodermal markers Xhox3 and Xcad1. However, co-expression of Smurf1 and Smad1 blocked induction of these markers at all Smurf1 doses tested, demonstrating that Smurf1 can antagonize Smad1 **activity**.
USE - Expression of (I) from (III) in a cell is useful for inhibiting a bone morphogenic protein (BMP) or transforming growth factor- beta (TGF beta) activation pathway in a cell (claimed). (I) is useful to block chondrogenesis, osteogenesis, blood differentiation, cartilage formation, neural tube patterning, retinal development, heart induction and morphogenesis, hair growth, tooth formation, gamete formation and a wide variety of tissue and organ formation processes, and hinder the regeneration, growth, maintenance, etc., of bone and other tissues that are dependent on the BMP pathway. (I) is useful for screening for various drugs and/or antibodies that can either enhance the BMP pathway, or inhibit it by antagonizing or mimicking the **activity** of (I), respectively, and in screening assays for identifying specific ligands of (I). (I) is useful as an immunogen to generate antibodies that are useful to alter the BMP pathway by inhibiting (I) or for diagnostic purposes. (I)

is useful for treating a disorder associated with BMP or TGF- beta activation, such as cancer. (I) or inhibitor of (I) can be delivered by a vector to modulate Smads, e.g. to prevent **Smurf** regulation of Smads where BMP or TGF beta **activity** is desired, such as in bone regeneration or to study **Smurf** regulator processes in vivo.
Dwg.0/18

ACCESSION NUMBER: 2001-071267 [08] WPIDS
DOC. NO. CPI: C2001-019969
TITLE: Novel isolated **Smurf** protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation.
DERWENT CLASS: B04 D16
INVENTOR(S): THOMSEN, G H; WRANA, J
PATENT ASSIGNEE(S): (HSCR-N) HSC RES & DEV LP; (UYNY) UNIV NEW YORK STATE RES FOUND
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000077168	A2	20001221	(200108)*	EN	106
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000056107	A	20010102	(200121)		
EP 1192174	A2	20020403	(200230)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003502064	W	20030121	(200308)		131
CN 1409722	A	20030409	(200345)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000077168	A2	WO 2000-US16250	20000612
AU 2000056107	A	AU 2000-56107	20000612
EP 1192174	A2	EP 2000-941398	20000612
		WO 2000-US16250	20000612
JP 2003502064	W	WO 2000-US16250	20000612
		JP 2001-504003	20000612
CN 1409722	A	CN 2000-811354	20000612

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000056107	A	Based on	WO 2000077168
EP 1192174	A2	Based on	WO 2000077168
JP 2003502064	W	Based on	WO 2000077168

PRIORITY APPLN. INFO: US 1999-138969P 19990611

L7 ANSWER 5 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory

Smad (I-**Smad**) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced **ubiquitination** and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their **ubiquitination** and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003:356072 BIOSIS
DOCUMENT NUMBER: PREV200300356072
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR(S): Murakami, Gyo; Watabe, Tetsuro; Takaoka, Kunio; Miyazono, Kohei [Reprint Author]; Imamura, Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo, 170-8455, Japan
miyazono-ind@umin.ac.jp
SOURCE: Molecular Biology of the Cell, (July 2003) Vol. 14, No. 7, pp. 2809-2817. print.
ISSN: 1059-1524 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 6 Aug 2003

L7 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation In addition, Smurf1 assocs. with transforming growth factor-β type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation Herein, we examined whether Smurf1 neg. regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced **ubiquitination** and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their **ubiquitination** and degradation Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003:571354 HCAPLUS
DOCUMENT NUMBER: 139:302479
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AUTHOR(S): Murakami, Gyo; Watabe, Tetsuro; Takaoka, Kunio; Miyazono, Kohei; Imamura, Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo, 170-8455, Japan
SOURCE: Molecular Biology of the Cell (2003), 14(7), 2809-2817
CODEN: MBCEEV; ISSN: 1059-1524
PUBLISHER: American Society for Cell Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

TI sequences human ubiquitin-protein synthetases as antagonists of BMP and TGF<b signaling pathways and expression during development and interactions with **Smad** proteins

AB This invention provides unique members of the Hect family of ubiquitin ligases that specifically target BMP and TGF<b/activin pathway-specific Smads. The novel ligases have been named Smurf1 and Smurf2. A transgenic expression system is described for these two proteins. They directly interact with Smads1 and 5 and Smad7, resp., and regulate the **ubiquitination**, turnover and **activity** of Smads and other proteins of these pathways. Smurf1 interferes with biol. responses to BMP, but not activin signaling. In amphibian embryos Smurf1 inhibits endogenous BMP signals, resulting in altered pattern formation and cell fate specification in the mesoderm and ectoderm. The present invention provides a unique regulatory link between the **ubiquitination** pathway and the control of cell fate determination by the TGF<b superfamily during embryonic development. Thus, Smurf1 is a neg. regulator of Smad1 signal transduction, by targeting Smad1, Smurf1 blocks BMP signaling. Screening assays which survey **Smurf** WW domain interaction with **Smad** protein PPXY domain are also relayed. In mammalian cells, Smurf2 suppresses TGF<b signaling, and in Xenopus, blocks formation of dorsal mesoderm and causes anterior truncation of the embryos. Smurf2 forms a stable complex with Smad7, which induces degradation and downregulation of TGF<b/activin signaling. The human Smurf1 gene was mapped to 7q21.1-q31.1.

ACCESSION NUMBER: 2000:900772 HCAPLUS
DOCUMENT NUMBER: 134:53133
TITLE: sequences human ubiquitin-protein synthetases as antagonists of BMP and TGF<b signaling pathways and expression during development and interactions with **Smad** proteins
INVENTOR(S): Thomsen, Gerald H.; Wrana, Jeffrey
PATENT ASSIGNEE(S): Research Foundation of State University of New York, USA; HSC Research and Development Limited Partnership
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077168	A2	20001221	WO 2000-US16250	20000612
WO 2000077168	A3	20010503		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000056107	A5	20010102	AU 2000-56107	20000612
EP 1192174	A2	20020403	EP 2000-941398	20000612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-138969P P 19990611
WO 2000-US16250 W 20000612

L7 ANSWER 8 OF 8 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads

AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation.
Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced **ubiquitination** and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their **ubiquitination** and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003:636252 SCISEARCH
THE GENUINE ARTICLE: 701CB
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AUTHOR: Murakami G; Watabe T; Takaoka K; Miyazono K (Reprint); Imamura T
CORPORATE SOURCE: Japanese Fdn Canc Res, Inst Canc, Dept Biochem, Tokyo 1708455, Japan (Reprint); Shinshu Univ, Dept Orthoped Surg, Nagano 3908621, Japan; Univ Tokyo, Dept Mol Pathol, Grad Sch Med, Tokyo 1130033, Japan; Osaka City Univ, Sch Med, Dept Orthoped Surg, Osaka 5458585, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (JUL 2003) Vol. 14, No. 7, pp. 2809-2817.
Publisher: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD 20814-2755 USA.
ISSN: 1059-1524.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 29
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

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(FILE 'HOME' ENTERED AT 17:00:20 ON 29 SEP 2004)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA, JICST-EPLUS, BIOTECHDS, BIOSIS, HCAPLUS, SCISEARCH, BIOBUSINESS, CEN, CEABA-VTB, JAPIO' ENTERED AT 17:01:06 ON 29 SEP 2004

L1 130 S SMURF
L2 48 S L1 AND ACTIVITY
L3 2 S SMURF ACTIVITY
L4 10848 S SMAD
L5 12 S L2 AND L4
L6 219 S L4 AND UBIQUITINATION
L7 8 S L5 AND L6

=> s Smurf WW domain
L8 2 SMURF WW DOMAIN

=> d l8 ti abs ibib tot

L8 ANSWER 1 OF 2 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
TI Novel isolated Smurf protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation.
AN 2001-071267 [08] WPIDS
AB WO 200077168 A UPAB: 20011129
NOVELTY - An isolated Smurf1 or Smurf2 protein (I), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid (II) encoding (I);

(2) a vector (III) comprising (II);

(3) a host cell (IV) comprising (III);

(4) production of (I);

(5) a transgenic non-human animal that expresses a human (I);

(6) screening (M) for a modulator of Smurf activity, comprising detecting modulation of Smurf activity in the presence of a test compound relative to Smurf activity in the absence of the test compound;

(7) an antibody (V) that specifically binds to (I);

(8) an oligonucleotide or nucleic acid (VI) that specifically hybridizes to (II) under highly stringent conditions; and

(9) promoting a bone morphogenic protein or transforming growth factor (TGF)- beta activation pathway in a cell, comprising suppressing expression of endogenous Smurf in the cell.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Negative regulator of Smad signal transduction; antagonist of BMP and TGF- beta signaling pathway.

The inhibition of Smad1 by Smurf1 was tested. By over expressing Smad1 and Smad2 together with various dosages of Smurf1 in Xenopus animal caps, the ability of Smurf1 to directly antagonize the mesoderm induction activities of Smad1 and Smad2, was tested. The results showed that expression of Smad1 alone induced ventral mesoderm, as demonstrated by expression of the ventral/posterior mesodermal markers Xhox3 and Xcad1. However, co-expression of Smurf1 and Smad1 blocked induction of these markers at all Smurf1 doses tested, demonstrating that Smurf1 can antagonize Smad1 activity.

USE - Expression of (I) from (III) in a cell is useful for inhibiting a bone morphogenic protein (BMP) or transforming growth factor- beta (TGF beta) activation pathway in a cell (claimed). (I) is useful to block chondrogenesis, osteogenesis, blood differentiation, cartilage formation, neural tube patterning, retinal development, heart induction and morphogenesis, hair growth, tooth formation, gamete formation and a wide variety of tissue and organ formation processes, and hinder the regeneration, growth, maintenance, etc., of bone and other tissues that are dependent on the BMP pathway. (I) is useful for screening for various drugs and/or antibodies that can either enhance the BMP pathway, or inhibit it by antagonizing or mimicking the activity of (I), respectively, and in screening assays for identifying specific ligands of (I). (I) is useful as an immunogen to generate antibodies that are useful to alter the BMP pathway by inhibiting (I) or for diagnostic purposes. (I) is useful for treating a disorder associated with BMP or TGF- beta activation, such as cancer. (I) or inhibitor of (I) can be delivered by a vector to modulate Smads, e.g. to prevent Smurf regulation of Smads where BMP or TGF beta activity is desired, such as in bone regeneration or to study Smurf regulator processes in vivo.

Dwg.0/18

ACCESSION NUMBER: 2001-071267 [08] WPIDS
DOC. NO. CPI: C2001-019969
TITLE: Novel isolated Smurf protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation.
DERWENT CLASS: B04 D16
INVENTOR(S): THOMSEN, G H; WRANA, J

PATENT ASSIGNEE(S): (HSCR-N) HSC RES & DEV LP; (UYNY) UNIV NEW YORK STATE RES FOUND
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000077168	A2	20001221	(200108)*	EN	106
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000056107	A	20010102	(200121)		
EP 1192174	A2	20020403	(200230)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003502064	W	20030121	(200308)		131
CN 1409722	A	20030409	(200345)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000077168	A2	WO 2000-US16250	20000612
AU 2000056107	A	AU 2000-56107	20000612
EP 1192174	A2	EP 2000-941398	20000612
		WO 2000-US16250	20000612
JP 2003502064	W	WO 2000-US16250	20000612
		JP 2001-504003	20000612
CN 1409722	A	CN 2000-811354	20000612

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000056107	A	Based on	WO 2000077168
EP 1192174	A2	Based on	WO 2000077168
JP 2003502064	W	Based on	WO 2000077168

PRIORITY APPLN. INFO: US 1999-138969P 19990611

L8 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
TI sequences human ubiquitin-protein synthetases as antagonists of BMP and TGF<b signaling pathways and expression during development and interactions with Smad proteins
AB This invention provides unique members of the Hect family of ubiquitin ligases that specifically target BMP and TGF<b/activin pathway-specific Smads. The novel ligases have been named Smurf1 and Smurf2. A transgenic expression system is described for these two proteins. They directly interact with Smads1 and 5 and Smad7, resp., and regulate the ubiquitination, turnover and activity of Smads and other proteins of these pathways. Smurf1 interferes with biol. responses to BMP, but not activin signaling. In amphibian embryos Smurf1 inhibits endogenous BMP signals, resulting in altered pattern formation and cell fate specification in the mesoderm and ectoderm. The present invention provides a unique regulatory link between the ubiquitination pathway and the control of cell fate determination by the TGF<b superfamily during embryonic development. Thus, Smurf1 is a neg. regulator of Smad1 signal transduction, by targeting Smad1, Smurf1 blocks BMP signaling. Screening assays which survey **Smurf WW domain** interaction with Smad protein PPXY domain are also relayed. In mammalian cells, Smurf2 suppresses TGF<b signaling, and

in Xenopus, blocks formation of dorsal mesoderm and causes anterior truncation of the embryos. Smurf2 forms a stable complex with Smad7, which induces degradation and downregulation of TGF<b/activin signaling. The human Smurf1 gene was mapped to 7q21.1-q31.1.

ACCESSION NUMBER: 2000:900772 HCAPLUS
DOCUMENT NUMBER: 134:53133
TITLE: sequences human ubiquitin-protein synthetases as antagonists of BMP and TGF<b signaling pathways and expression during development and interactions with Smad proteins
INVENTOR(S): Thomsen, Gerald H.; Wrana, Jeffrey
PATENT ASSIGNEE(S): Research Foundation of State University of New York, USA; HSC Research and Development Limited Partnership
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077168	A2	20001221	WO 2000-US16250	20000612
WO 2000077168	A3	20010503		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000056107	A5	20010102	AU 2000-56107	20000612
EP 1192174	A2	20020403	EP 2000-941398	20000612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:
US 1999-138969P P 19990611
WO 2000-US16250 W 20000612

=> s PPYX
L9 1 PPYX

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L9 ANSWER 1 OF 1 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Toward genolelectronics: Nucleic acid doped conducting polymers
AB New biocomposite materials, based on the incorporation of nucleic acid dopants within an electronically conducting polypyrrole network, are described. The growth patterns and ion-exchange properties of these electropolymerized polypyrrole-oligonucleotide (PPy/ODN) films are characterized using an in situ electrochemical quartz crystal microbalance (EQCM). The EQCM and corresponding voltammetric data indicate that nucleic acids can serve as the sole charge-compensating counterions during the film formation. While the incorporation of ODNs is similar to that of small inorganic anions, such large nucleic acid dopants could not be readily expelled from the PPy network. As a result, the electrochemistry is dominated by the movement of the electrolyte cation:
PPy(ODNn-)(X)(Na+)(nX)double left right arrow **PPyX**
+(ODn-)(X)+nxNa(+)nxe(-)
Various parameters, such as the ODN length or concentration and the potential range, have a marked effect on the properties of the new

conducting biomaterials. Very favorable growth patterns are observed for biocomposites containing 20-30-mer long ODNs, while films based on shorter oligonucleotides or chromosomal DNA display inferior properties. The composite films can be prepared using low (similar to 1 x 10(-5) M) concentrations of the nucleic acid dopant, in the absence of additional electrolyte. Such biomaterials open up new opportunities, including genoelectronic devices, composite materials, bioactive interfaces, genetic analysis, or probing of DNA charge transfer.

ACCESSION NUMBER: 2000:198773 SCISEARCH
THE GENUINE ARTICLE: 290NB
TITLE: Toward genolelectronics: Nucleic acid doped conducting polymers
AUTHOR: Wang J (Reprint); Jiang M
CORPORATE SOURCE: NEW MEXICO STATE UNIV, DEPT CHEM & BIOCHEM, LAS CRUCES, NM 88003 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: LANGMUIR, (7 MAR 2000) Vol. 16, No. 5, pp. 2269-2274. Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036. ISSN: 0743-7463.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 19
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

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(FILE 'HOME' ENTERED AT 17:00:20 ON 29 SEP 2004)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA, JICST-EPLUS, BIOTECHDS, BIOSIS, HCAPLUS, SCISEARCH, BIOBUSINESS, CEN, CEABA-VTB, JAPIO' ENTERED AT 17:01:06 ON 29 SEP 2004

L1 130 S SMURF
L2 48 S L1 AND ACTIVITY
L3 2 S SMURF ACTIVITY
L4 10848 S SMAD
L5 12 S L2 AND L4
L6 219 S L4 AND UBIQUITINATION
L7 8 S L5 AND L6
L8 2 S SMURF WW DOMAIN
L9 1 S PPYX

=> s PPYY domain
L10 0 PPYY DOMAIN

=> s PPYX domain
L11 0 PPYX DOMAIN

=> d l9 ti abs ibib tot

L9 ANSWER 1 OF 1 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Toward genolelectronics: Nucleic acid doped conducting polymers
AB New biocomposite materials, based on the incorporation of nucleic acid dopants within an electronically conducting polypyrrole network, are described. The growth patterns and ion-exchange properties of these electropolymerized polypyrrole-oligonucleotide (PPy/ODN) films are characterized using an in situ electrochemical quartz crystal microbalance (EQCM). The EQCM and corresponding voltammetric data indicate that nucleic acids can serve as the sole charge-compensating counterions during the film formation. While the incorporation of ODNs is similar to that of small inorganic anions, such large nucleic acid dopants could not be

readily expelled from the PPy network. As a result, the electrochemistry is dominated by the movement of the electrolyte cation:
PPy(ODNn-)(X)(Na+)(nX)double left right arrow **PPyX**
+(ODn-)(X)+nxNa(+)nxe(-)
Various parameters, such as the ODN length or concentration and the potential range, have a marked effect on the properties of the new conducting biomaterials. Very favorable growth patterns are observed for biocomposites containing 20-30-mer long ODNs, while films based on shorter oligonucleotides or chromosomal DNA display inferior properties. The composite films can be prepared using low (similar to 1 x 10(-5) M) concentrations of the nucleic acid dopant, in the absence of additional electrolyte. Such biomaterials open up new opportunities, including genoelectronic devices, composite materials, bioactive interfaces, genetic analysis, or probing of DNA charge transfer.

ACCESSION NUMBER: 2000:198773 SCISEARCH
THE GENUINE ARTICLE: 290NB
TITLE: Toward genolelectronics: Nucleic acid doped conducting polymers
AUTHOR: Wang J (Reprint); Jiang M
CORPORATE SOURCE: NEW MEXICO STATE UNIV, DEPT CHEM & BIOCHEM, LAS CRUCES, NM 88003 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: LANGMUIR, (7 MAR 2000) Vol. 16, No. 5, pp. 2269-2274. Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036. ISSN: 0743-7463.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 19
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

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=> e thomsen, g
E1            2     THOMSEM/BI
E2         4283     THOMSEN/BI
E3            0 --> THOMSEN, G/BI
E4            4     THOMSENA/BI
E5            1     THOMSENAE/BI
E6            1     THOMSENALITE/BI
E7            1     THOMSENCONVENT/BI
E8            1     THOMSENFRIEDENREICH/BI
E9           10     THOMSENI/BI
E10           3     THOMSENIEN/BI
E11           5     THOMSENII/BI
E12          49     THOMSENOLITE/BI

=> e wrana, j/au
E1            1     WRANA R O/AU
E2            1     WRANA W/AU
E3            0 --> WRANA, J/AU
E4            1     WRANAN GUIDO VON/AU
E5            1     WRANAWIN K/AU
E6            1     WRANCE O/AU
E7            1     WRANCKEN A/AU
E8            1     WRANEK J/AU
E9            1     WRANEK P/AU
E10          57     WRANEK U/AU
E11           3     WRANEK URSULA/AU
E12           2     WRANELL L/AU

=> s e2
L12           1 "WRANA W"/AU
```

```
=> d l12 ti abs ibib tot

L12  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
TI   The strength and beating of paper pulps
AB   An illustrated lecture.
ACCESSION NUMBER:         1943:32621  HCAPLUS
DOCUMENT NUMBER:          37:32621
ORIGINAL REFERENCE NO.:   37:5235d
TITLE:                    The strength and beating of paper pulps
AUTHOR(S):                Wrana, W.
SOURCE:                   Papierfabrikant (1942), 40, 215-20
                          CODEN: PAFAAM
DOCUMENT TYPE:            Journal
LANGUAGE:                 Unavailable


=> d his

     (FILE 'HOME' ENTERED AT 17:00:20 ON 29 SEP 2004)

     FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA, JICST-EPLUS,
     BIOTECHDS, BIOSIS, HCAPLUS, SCISEARCH, BIOBUSINESS, CEN, CEABA-VTB,
     JAPIO' ENTERED AT 17:01:06 ON 29 SEP 2004
L1           130 S SMURF
L2            48 S L1 AND ACTIVITY
L3             2 S SMURF ACTIVITY
L4         10848 S SMAD
L5            12 S L2 AND L4
L6           219 S L4 AND UBIQUITINATION
L7             8 S L5 AND L6
L8             2 S SMURF WW DOMAIN
L9             1 S PPYX
L10            0 S PPYY DOMAIN
L11            0 S PPYX DOMAIN
                 E THOMSEN, G
                 E WRANA, J/AU
L12            1 S E2
```

d l5 ti abs ibib tot

L5 ANSWER 1 OF 12 MEDLINE on STN

TI Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.

AB The Runt domain transcription factors (RUNXs) play essential roles in normal development and neoplasias. Genetic analyses of animals and humans have revealed the involvement of RUNX1 in hematopoiesis and leukemia, RUNX2 in osteogenesis and cleidocranial dysplasia, and RUNX3 in the development of T-cells and dorsal root ganglion neurons and in the genesis of gastric cancer. Here we report that RUNX3 is a target of the acetyltransferase **activity** of p300. The p300-dependent acetylation of three lysine residues protects RUNX3 from ubiquitin ligase **Smurf**-mediated degradation. The extent of the acetylation is up-regulated by the transforming growth factor-beta signaling pathway and down-regulated by histone deacetylase activities. Our findings demonstrate that the level of RUNX3 protein is controlled by the competitive acetylation and deacetylation of the three lysine residues, revealing a new mechanism for the posttranslational regulation of RUNX3 expression.

ACCESSION NUMBER: 2004349788 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15138260
TITLE: Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.
AUTHOR: Jin Yun-Hye; Jeon Eun-Joo; Li Qing-Lin; Lee Yong Hee; Choi Joong-Kook; Kim Wun-Jae; Lee Kwang-Youl; Bae Suk-Chul
CORPORATE SOURCE: Department of Biochemistry and Urology, School of Medicine and Institute for Tumor Research, Chungbuk National University, Cheongju 361-763, South Korea.
SOURCE: Journal of biological chemistry, (2004 Jul 9) 279 (28) 29409-17.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040716
Last Updated on STN: 20040825
Entered Medline: 20040824

L5 ANSWER 2 OF 12 MEDLINE on STN

TI Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts.

AB The principal effect of TGF-beta1 on mesenchymal cells is its stimulation of ECM synthesis. Previous reports indicated the significance of the autocrine TGF-beta loop in the pathogenesis of scleroderma. In this study, we focused on Smad7 and Smurfs, principal molecules in the negative regulation of TGF-beta signaling, to further understand the autocrine TGF-beta loop in scleroderma. Scleroderma fibroblasts exhibited increased Smad7 levels compared with normal fibroblasts in vivo and in vitro. Smad7 constitutively formed a complex with the TGF-beta receptors, and the inhibitory effect of Smad7 on the promoter **activity** of human alpha2(I) collagen and 3TP-lux was completely impaired in scleroderma fibroblasts. Furthermore, the protein stability of TGF-beta receptor type I was significantly increased in scleroderma fibroblasts compared with normal fibroblasts. There was no significant difference in Smurf1 and Smurf2 levels between normal and scleroderma fibroblasts, and the transiently overexpressed Smurf1 and/or Smurf2 did not affect TGF-beta receptor type I protein levels in scleroderma fibroblasts. These results indicate that the impaired Smad7-**Smurf**-mediated inhibitory effect on TGF-beta signaling might contribute to maintaining the autocrine TGF-beta loop in scleroderma fibroblasts. To our knowledge, this is the

first report of a disturbed negative regulation of TGF-beta signaling in fibrotic disorders.

ACCESSION NUMBER: 2004023363 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14722617
TITLE: Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts.
AUTHOR: Asano Yoshihide; Ihn Hironobu; Yamane Kenichi; Kubo Masahide; Tamaki Kunihiko
CORPORATE SOURCE: Department of Dermatology, Faculty of Medicine, University of Tokyo, Tokyo, Japan.
SOURCE: Journal of clinical investigation, (2004 Jan) 113 (2) 253-64.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20040115
Last Updated on STN: 20040210
Entered Medline: 20040209

L5 ANSWER 3 OF 12 MEDLINE on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003328281 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12857866
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR: Murakami Gyo; Watabe Tetsuro; Takaoka Kunio; Miyazono Kohei; Imamura Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo 170-8455, Japan.
SOURCE: Molecular biology of the cell, (2003 Jul) 14 (7) 2809-17.
Journal code: 9201390. ISSN: 1059-1524.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20030715
Last Updated on STN: 20040414
Entered Medline: 20040413

L5 ANSWER 4 OF 12 EMBASE
on STN

TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.

AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-β type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003293267 EMBASE
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR: Murakami G.; Watabe T.; Takaoka K.; Miyazono K.; Imamura T.
CORPORATE SOURCE: K. Miyazono, Department of Biochemistry, Cancer Inst. Japan. Found. Cancer R., Tokyo 170-8455, Japan. miyazono-ind@umin.ac.jp
SOURCE: Molecular Biology of the Cell, (1 Jul 2003) 14/7 (2809-2817).
Refs: 29
ISSN: 1059-1524 CODEN: MBCEEV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L5 ANSWER 5 OF 12 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN

TI Identifying protein-protein interactions, useful e.g. in drug development, comprises introducing into cells one or more prey proteins labeled with an epitope tag and one or more bait proteins labeled with a detectable substance.

AN 2004-315601 [29] WPIDS

AB WO2004023146 A UPAB: 20040505
NOVELTY - Identifying protein-protein interactions comprising prey proteins interacting with one or more bait comprises introducing one or more prey proteins in labeled with an epitope tag and one or more bait protein in cells labeled with a detectable substance.

DETAILED DESCRIPTION - Identifying protein-protein interactions comprising prey proteins interacting with one or more bait comprises:

(a) introducing one or more prey proteins in cells, where a prey is labeled with an epitope tag permitting separation of the prey protein from other proteins in the cells;

(b) introducing one or more bait protein in cells, where a bait protein is labeled with a detectable substance permitting detection of the bait protein and protein-protein interactions comprising a prey protein and the bait protein;

(c) inducing formation of protein-protein interactions between a prey and bait protein; and

(d) assaying for protein-protein interactions comprising a prey protein and bait protein by detecting the detectable substance.

INDEPENDENT CLAIMS are also included for:

(1) quantitating protein-protein interactions;

(2) determining an interactome for one or more bait protein;

(3) determining the functions of gene product;

(4) systematically and quantitatively analyzing protein-protein interactions in cell signaling;

(5) determining the changes in an interactome of mitotic kinase during cell cycle progression;

(6) analyzing protein-protein interactions in different cell types;

(7) assaying for changes in protein-protein interactions in response to intracellular and extracellular factors;

(8) identifying a potential modulator of signal transduction **activity**; and

(9) an agent, modulator or inhibitor identified by a method of (8).

ACTIVITY - Antiinflammatory; Cytostatic.

No biological data given.

MECHANISM OF ACTION - None Given.

USE - The method and kits are useful in identifying, quantifying and analyzing protein-protein interactions. The method is useful in determining a disease or condition associated with a test protein, monitoring the course of therapy, conducting a drug discovery business and in detecting mutations in cellular proteins. The pharmaceutical composition is useful in treating and preventing a disease or condition associated with an abnormality in a signal transduction pathway, e.g. fibrosis, inflammation or cancer.

Dwg.0/3

ACCESSION NUMBER: 2004-315601 [29] WPIDS
DOC. NO. NON-CPI: N2004-251489
DOC. NO. CPI: C2004-119632
TITLE: Identifying protein-protein interactions, useful e.g. in drug development, comprises introducing into cells one or more prey proteins labeled with an epitope tag and one or more bait proteins labeled with a detectable substance.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BARRIOS-RODILES, M; WRANA, J
PATENT ASSIGNEE(S): (MOUN) MOUNT SINAI HOSPITAL
COUNTRY COUNT: 105
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004023146	A2	20040318	(200429)*	EN	53
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003264211	A1	20040329	(200459)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004023146	A2	WO 2003-CA1354	20030905
AU 2003264211	A1	AU 2003-264211	20030905

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003264211	A1 Based on	WO 2004023146

PRIORITY APPLN. INFO: US 2002-408922P 20020906

L5 ANSWER 6 OF 12 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
TI Novel isolated **Smurf** protein useful for inhibiting bone

morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation.

AN 2001-071267 [08] WPIDS

AB WO 200077168 A UPAB: 20011129

NOVELTY - An isolated Smurf1 or Smurf2 protein (I), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid (II) encoding (I);

(2) a vector (III) comprising (II);

(3) a host cell (IV) comprising (III);

(4) production of (I);

(5) a transgenic non-human animal that expresses a human (I);

(6) screening (M) for a modulator of **Smurf activity**, comprising detecting modulation of **Smurf activity** in the presence of a test compound relative to **Smurf activity** in the absence of the test compound;

(7) an antibody (V) that specifically binds to (I);

(8) an oligonucleotide or nucleic acid (VI) that specifically hybridizes to (II) under highly stringent conditions; and

(9) promoting a bone morphogenic protein or transforming growth factor (TGF)- beta activation pathway in a cell, comprising suppressing expression of endogenous **Smurf** in the cell.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Negative regulator of **Smad** signal transduction; antagonist of BMP and TGF- beta signaling pathway.

The inhibition of Smad1 by Smurf1 was tested. By over expressing Smad1 and Smad2 together with various dosages of Smurf1 in Xenopus animal caps, the ability of Smurf1 to directly antagonize the mesoderm induction activities of Smad1 and Smad2, was tested. The results showed that expression of Smad1 alone induced ventral mesoderm, as demonstrated by expression of the ventral/posterior mesodermal markers Xhox3 and Xcad1. However, co-expression of Smurf1 and Smad1 blocked induction of these markers at all Smurf1 doses tested, demonstrating that Smurf1 can antagonize Smad1 **activity**.

USE - Expression of (I) from (III) in a cell is useful for inhibiting a bone morphogenic protein (BMP) or transforming growth factor- beta (TGF beta) activation pathway in a cell (claimed). (I) is useful to block chondrogenesis, osteogenesis, blood differentiation, cartilage formation, neural tube patterning, retinal development, heart induction and morphogenesis, hair growth, tooth formation, gamete formation and a wide variety of tissue and organ formation processes, and hinder the regeneration, growth, maintenance, etc., of bone and other tissues that are dependent on the BMP pathway. (I) is useful for screening for various drugs and/or antibodies that can either enhance the BMP pathway, or inhibit it by antagonizing or mimicking the **activity** of (I), respectively, and in screening assays for identifying specific ligands of (I). (I) is useful as an immunogen to generate antibodies that are useful to alter the BMP pathway by inhibiting (I) or for diagnostic purposes. (I) is useful for treating a disorder associated with BMP or TGF- beta activation, such as cancer. (I) or inhibitor of (I) can be delivered by a vector to modulate Smads, e.g. to prevent **Smurf** regulation of Smads where BMP or TGF beta **activity** is desired, such as in bone regeneration or to study **Smurf** regulator processes in vivo.

Dwg.0/18

ACCESSION NUMBER: 2001-071267 [08] WPIDS

DOC. NO. CPI: C2001-019969

TITLE: Novel isolated **Smurf** protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation.

DERWENT CLASS: B04 D16

INVENTOR(S): THOMSEN, G H; WRANA, J

PATENT ASSIGNEE(S): (HSCR-N) HSC RES & DEV LP; (UYNY) UNIV NEW YORK STATE RES FOUND

COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000077168	A2	20001221	(200108)*	EN	106
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000056107	A	20010102	(200121)		
EP 1192174	A2	20020403	(200230)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003502064	W	20030121	(200308)		131
CN 1409722	A	20030409	(200345)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000077168	A2	WO 2000-US16250	20000612
AU 2000056107	A	AU 2000-56107	20000612
EP 1192174	A2	EP 2000-941398	20000612
		WO 2000-US16250	20000612
JP 2003502064	W	WO 2000-US16250	20000612
		JP 2001-504003	20000612
CN 1409722	A	CN 2000-811354	20000612

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000056107	A	Based on	WO 2000077168
EP 1192174	A2	Based on	WO 2000077168
JP 2003502064	W	Based on	WO 2000077168

PRIORITY APPLN. INFO: US 1999-138969P 19990611

L5 ANSWER 7 OF 12 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.

AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003:356072 BIOSIS
DOCUMENT NUMBER: PREV200300356072

TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR(S): Murakami, Gyo; Watabe, Tetsuro; Takaoka, Kunio; Miyazono, Kohei [Reprint Author]; Imamura, Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo, 170-8455, Japan
miyazono-ind@umin.ac.jp
SOURCE: Molecular Biology of the Cell, (July 2003) Vol. 14, No. 7, pp. 2809-2817. print.
ISSN: 1059-1524 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 6 Aug 2003

L5 ANSWER 8 OF 12 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Specificity and complexity in **Smurf**-mediated **Smad** degradation.
ACCESSION NUMBER: 2002:133151 BIOSIS
DOCUMENT NUMBER: PREV200200133151
TITLE: Specificity and complexity in **Smurf**-mediated **Smad** degradation.
AUTHOR(S): Liang, Min [Reprint author]; Lin, Xia [Reprint author]; Liang, Yao-Yun [Reprint author]; Feng, Xin-Hua [Reprint author]; DeBakey, Michael E. [Reprint author]
CORPORATE SOURCE: Department of Surgery, Baylor College of Medicine, One Baylor Plaza, 139D, Houston, TX, 77030, USA
SOURCE: Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. Supplement, pp. 148a. print.
Meeting Info.: 41st Annual Meeting of the American Society for Cell Biology. Washington DC, USA. December 08-12, 2001. American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Feb 2002
Last Updated on STN: 26 Feb 2002

L5 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
TI Impaired Smad7-**Smurf**-mediated negative regulation of TGF-β signaling in scleroderma fibroblasts
AB The principal effect of TGF-β1 on mesenchymal cells is its stimulation of ECM synthesis. Previous reports indicated the significance of the autocrine TGF-β loop in the pathogenesis of scleroderma. In this study, the authors focused on Smad7 and Smurfs, principal mols. in the neg. regulation of TGF-β signaling, to further understand the autocrine TGF-β loop in scleroderma. Scleroderma fibroblasts exhibited increased Smad7 levels compared with normal fibroblasts in vivo and in vitro. Smad7 constitutively formed a complex with the TGF-β receptors, and the inhibitory effect of Smad7 on the promoter **activity** of human α2(I) collagen and 3TP-lux was completely impaired in scleroderma fibroblasts. Furthermore, the protein stability of TGF-β receptor type I was significantly increased in scleroderma fibroblasts compared with normal fibroblasts. There was no significant difference in Smurf1 and Smurf2 levels between normal and scleroderma fibroblasts, and the transiently overexpressed Smurf1 and/or Smurf2 did not affect TGF-β receptor type I protein levels in scleroderma fibroblasts. These results indicate that the impaired Smad7-**Smurf** -mediated inhibitory effect on TGF-β signaling might contribute to maintaining the autocrine TGF-β loop in scleroderma fibroblasts. To our knowledge, this is the first report of a disturbed neg. regulation of

TGF-β signaling in fibrotic disorders.

ACCESSION NUMBER: 2004:64890 HCAPLUS
DOCUMENT NUMBER: 140:216014
TITLE: Impaired Smad7-**Smurf**-mediated negative regulation of TGF-β signaling in scleroderma fibroblasts
AUTHOR(S): Asano, Yoshihide; Ihn, Hironobu; Yamane, Kenichi; Kubo, Masahide; Tamaki, Kunihiko
CORPORATE SOURCE: Department of Dermatology, Faculty of Medicine, University of Tokyo, Tokyo, Japan
SOURCE: Journal of Clinical Investigation (2004), 113(2), 253-264
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation In addition, Smurf1 assocs. with transforming growth factor-β type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation Herein, we examined whether Smurf1 neg. regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003:571354 HCAPLUS
DOCUMENT NUMBER: 139:302479
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AUTHOR(S): Murakami, Gyo; Watabe, Tetsuro; Takaoka, Kunio; Miyazono, Kohei; Imamura, Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo, 170-8455, Japan
SOURCE: Molecular Biology of the Cell (2003), 14(7), 2809-2817
CODEN: MBCEEV; ISSN: 1059-1524
PUBLISHER: American Society for Cell Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
TI sequences human ubiquitin-protein synthetases as antagonists of BMP and TGF<b signaling pathways and expression during development and interactions with **Smad** proteins
AB This invention provides unique members of the Hect family of ubiquitin ligases that specifically target BMP and TGF<b/activin pathway-specific Smads. The novel ligases have been named Smurf1 and Smurf2. A transgenic expression system is described for these two proteins. They directly interact with Smads1 and 5 and Smad7, resp., and regulate the

ubiquitination, turnover and **activity** of Smads and other proteins of these pathways. Smurf1 interferes with biol. responses to BMP, but not activin signaling. In amphibian embryos Smurf1 inhibits endogenous BMP signals, resulting in altered pattern formation and cell fate specification in the mesoderm and ectoderm. The present invention provides a unique regulatory link between the ubiquitination pathway and the control of cell fate determination by the TGF<b superfamily during embryonic development. Thus, Smurf1 is a neg. regulator of Smad1 signal transduction, by targeting Smad1, Smurf1 blocks BMP signaling. Screening assays which survey **Smurf** WW domain interaction with **Smad** protein PPXY domain are also relayed. In mammalian cells, Smurf2 suppresses TGF<b signaling, and in Xenopus, blocks formation of dorsal mesoderm and causes anterior truncation of the embryos. Smurf2 forms a stable complex with Smad7, which induces degradation and downregulation of TGF<b/activin signaling. The human Smurf1 gene was mapped to 7q21.1-q31.1.

ACCESSION NUMBER: 2000:900772 HCAPLUS
DOCUMENT NUMBER: 134:53133
TITLE: sequences human ubiquitin-protein synthetases as antagonists of BMP and TGF<b signaling pathways and expression during development and interactions with **Smad** proteins
INVENTOR(S): Thomsen, Gerald H.; Wrana, Jeffrey
PATENT ASSIGNEE(S): Research Foundation of State University of New York, USA; HSC Research and Development Limited Partnership
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077168	A2	20001221	WO 2000-US16250	20000612
WO 2000077168	A3	20010503		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000056107	A5	20010102	AU 2000-56107	20000612
EP 1192174	A2	20020403	EP 2000-941398	20000612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:	US 1999-138969P	P	19990611
	WO 2000-US16250	W	20000612

L5 ANSWER 12 OF 12 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads

AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced

secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003:636252 SCISEARCH
THE GENUINE ARTICLE: 701CB
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AUTHOR: Murakami G; Watabe T; Takaoka K; Miyazono K (Reprint); Imamura T
CORPORATE SOURCE: Japanese Fdn Canc Res, Inst Canc, Dept Biochem, Tokyo 1708455, Japan (Reprint); Shinshu Univ, Dept Orthoped Surg, Nagano 3908621, Japan; Univ Tokyo, Dept Mol Pathol, Grad Sch Med, Tokyo 1130033, Japan; Osaka City Univ, Sch Med, Dept Orthoped Surg, Osaka 5458585, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (JUL 2003) Vol. 14, No. 7, pp. 2809-2817.
Publisher: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD 20814-2755 USA.
ISSN: 1059-1524.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 29
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

=>

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L5 ANSWER 1 OF 12 MEDLINE on STN

TI Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.

AB The Runt domain transcription factors (RUNXs) play essential roles in normal development and neoplasias. Genetic analyses of animals and humans have revealed the involvement of RUNX1 in hematopoiesis and leukemia, RUNX2 in osteogenesis and cleidocranial dysplasia, and RUNX3 in the development of T-cells and dorsal root ganglion neurons and in the genesis of gastric cancer. Here we report that RUNX3 is a target of the acetyltransferase **activity** of p300. The p300-dependent acetylation of three lysine residues protects RUNX3 from ubiquitin ligase **Smurf**-mediated degradation. The extent of the acetylation is up-regulated by the transforming growth factor-beta signaling pathway and down-regulated by histone deacetylase activities. Our findings demonstrate that the level of RUNX3 protein is controlled by the competitive acetylation and deacetylation of the three lysine residues, revealing a new mechanism for the posttranslational regulation of RUNX3 expression.

ACCESSION NUMBER: 2004349788 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15138260
TITLE: Transforming growth factor-beta stimulates p300-dependent RUNX3 acetylation, which inhibits ubiquitination-mediated degradation.
AUTHOR: Jin Yun-Hye; Jeon Eun-Joo; Li Qing-Lin; Lee Yong Hee; Choi Joong-Kook; Kim Wun-Jae; Lee Kwang-Youl; Bae Suk-Chul
CORPORATE SOURCE: Department of Biochemistry and Urology, School of Medicine and Institute for Tumor Research, Chungbuk National University, Cheongju 361-763, South Korea.
SOURCE: Journal of biological chemistry, (2004 Jul 9) 279 (28) 29409-17.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040716
Last Updated on STN: 20040825
Entered Medline: 20040824

L5 ANSWER 2 OF 12 MEDLINE on STN

TI Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts.

AB The principal effect of TGF-beta1 on mesenchymal cells is its stimulation of ECM synthesis. Previous reports indicated the significance of the autocrine TGF-beta loop in the pathogenesis of scleroderma. In this study, we focused on Smad7 and Smurfs, principal molecules in the negative regulation of TGF-beta signaling, to further understand the autocrine TGF-beta loop in scleroderma. Scleroderma fibroblasts exhibited increased Smad7 levels compared with normal fibroblasts in vivo and in vitro. Smad7 constitutively formed a complex with the TGF-beta receptors, and the inhibitory effect of Smad7 on the promoter **activity** of human alpha2(I) collagen and 3TP-lux was completely impaired in scleroderma fibroblasts. Furthermore, the protein stability of TGF-beta receptor type I was significantly increased in scleroderma fibroblasts compared with normal fibroblasts. There was no significant difference in Smurf1 and Smurf2 levels between normal and scleroderma fibroblasts, and the transiently overexpressed Smurf1 and/or Smurf2 did not affect TGF-beta receptor type I protein levels in scleroderma fibroblasts. These results indicate that the impaired Smad7-**Smurf**-mediated inhibitory effect on TGF-beta signaling might contribute to maintaining the autocrine TGF-beta loop in scleroderma fibroblasts. To our knowledge, this is the

first report of a disturbed negative regulation of TGF-beta signaling in fibrotic disorders.

ACCESSION NUMBER: 2004023363 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14722617
TITLE: Impaired Smad7-**Smurf**-mediated negative regulation of TGF-beta signaling in scleroderma fibroblasts.
AUTHOR: Asano Yoshihide; Ihn Hironobu; Yamane Kenichi; Kubo Masahide; Tamaki Kunihiko
CORPORATE SOURCE: Department of Dermatology, Faculty of Medicine, University of Tokyo, Tokyo, Japan.
SOURCE: Journal of clinical investigation, (2004 Jan) 113 (2) 253-64.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20040115
Last Updated on STN: 20040210
Entered Medline: 20040209

L5 ANSWER 3 OF 12 MEDLINE on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003328281 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12857866
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR: Murakami Gyo; Watabe Tetsuro; Takaoka Kunio; Miyazono Kohei; Imamura Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo 170-8455, Japan.
SOURCE: Molecular biology of the cell, (2003 Jul) 14 (7) 2809-17.
Journal code: 9201390. ISSN: 1059-1524.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20030715
Last Updated on STN: 20040414
Entered Medline: 20040413

L5 ANSWER 4 OF 12 EMBASE
on STN

TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.

AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-β type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003293267 EMBASE
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR: Murakami G.; Watabe T.; Takaoka K.; Miyazono K.; Imamura T.
CORPORATE SOURCE: K. Miyazono, Department of Biochemistry, Cancer Inst. Japan. Found. Cancer R., Tokyo 170-8455, Japan. miyazono-ind@umin.ac.jp
SOURCE: Molecular Biology of the Cell, (1 Jul 2003) 14/7 (2809-2817).
Refs: 29
ISSN: 1059-1524 CODEN: MBCEEV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L5 ANSWER 5 OF 12 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN

TI Identifying protein-protein interactions, useful e.g. in drug development, comprises introducing into cells one or more prey proteins labeled with an epitope tag and one or more bait proteins labeled with a detectable substance.

AN 2004-315601 [29] WPIDS
AB WO2004023146 A UPAB: 20040505

NOVELTY - Identifying protein-protein interactions comprising prey proteins interacting with one or more bait comprises introducing one or more prey proteins in labeled with an epitope tag and one or more bait protein in cells labeled with a detectable substance.

DETAILED DESCRIPTION - Identifying protein-protein interactions comprising prey proteins interacting with one or more bait comprises:

(a) introducing one or more prey proteins in cells, where a prey is labeled with an epitope tag permitting separation of the prey protein from other proteins in the cells;

(b) introducing one or more bait protein in cells, where a bait protein is labeled with a detectable substance permitting detection of the bait protein and protein-protein interactions comprising a prey protein and the bait protein;

(c) inducing formation of protein-protein interactions between a prey and bait protein; and

(d) assaying for protein-protein interactions comprising a prey protein and bait protein by detecting the detectable substance.

INDEPENDENT CLAIMS are also included for:

(1) quantitating protein-protein interactions;

(2) determining an interactome for one or more bait protein;

(3) determining the functions of gene product;

(4) systematically and quantitatively analyzing protein-protein interactions in cell signaling;

(5) determining the changes in an interactome of mitotic kinase during cell cycle progression;

(6) analyzing protein-protein interactions in different cell types;

(7) assaying for changes in protein-protein interactions in response to intracellular and extracellular factors;

(8) identifying a potential modulator of signal transduction **activity**; and

(9) an agent, modulator or inhibitor identified by a method of (8).

ACTIVITY - Antiinflammatory; Cytostatic.

No biological data given.

MECHANISM OF ACTION - None Given.

USE - The method and kits are useful in identifying, quantifying and analyzing protein-protein interactions. The method is useful in determining a disease or condition associated with a test protein, monitoring the course of therapy, conducting a drug discovery business and in detecting mutations in cellular proteins. The pharmaceutical composition is useful in treating and preventing a disease or condition associated with an abnormality in a signal transduction pathway, e.g. fibrosis, inflammation or cancer.

Dwg.0/3

ACCESSION NUMBER: 2004-315601 [29] WPIDS
DOC. NO. NON-CPI: N2004-251489
DOC. NO. CPI: C2004-119632
TITLE: Identifying protein-protein interactions, useful e.g. in drug development, comprises introducing into cells one or more prey proteins labeled with an epitope tag and one or more bait proteins labeled with a detectable substance.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BARRIOS-RODILES, M; WRANA, J
PATENT ASSIGNEE(S): (MOUN) MOUNT SINAI HOSPITAL
COUNTRY COUNT: 105
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004023146	A2	20040318	(200429)*	EN	53
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003264211	A1	20040329	(200459)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004023146	A2	WO 2003-CA1354	20030905
AU 2003264211	A1	AU 2003-264211	20030905

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003264211	A1 Based on	WO 2004023146

PRIORITY APPLN. INFO: US 2002-408922P 20020906

L5 ANSWER 6 OF 12 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
TI Novel isolated **Smurf** protein useful for inhibiting bone

morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation.

AN 2001-071267 [08] WPIDS

AB WO 200077168 A UPAB: 20011129

NOVELTY - An isolated Smurf1 or Smurf2 protein (I), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid (II) encoding (I);

(2) a vector (III) comprising (II);

(3) a host cell (IV) comprising (III);

(4) production of (I);

(5) a transgenic non-human animal that expresses a human (I);

(6) screening (M) for a modulator of **Smurf activity**, comprising detecting modulation of **Smurf activity** in the presence of a test compound relative to **Smurf activity** in the absence of the test compound;

(7) an antibody (V) that specifically binds to (I);

(8) an oligonucleotide or nucleic acid (VI) that specifically hybridizes to (II) under highly stringent conditions; and

(9) promoting a bone morphogenic protein or transforming growth factor (TGF)- beta activation pathway in a cell, comprising suppressing expression of endogenous **Smurf** in the cell.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Negative regulator of **Smad** signal transduction; antagonist of BMP and TGF- beta signaling pathway.

The inhibition of Smad1 by Smurf1 was tested. By over expressing Smad1 and Smad2 together with various dosages of Smurf1 in Xenopus animal caps, the ability of Smurf1 to directly antagonize the mesoderm induction activities of Smad1 and Smad2, was tested. The results showed that expression of Smad1 alone induced ventral mesoderm, as demonstrated by expression of the ventral/posterior mesodermal markers Xhox3 and Xcad1. However, co-expression of Smurf1 and Smad1 blocked induction of these markers at all Smurf1 doses tested, demonstrating that Smurf1 can antagonize Smad1 **activity**.

USE - Expression of (I) from (III) in a cell is useful for inhibiting a bone morphogenic protein (BMP) or transforming growth factor- beta (TGF beta) activation pathway in a cell (claimed). (I) is useful to block chondrogenesis, osteogenesis, blood differentiation, cartilage formation, neural tube patterning, retinal development, heart induction and morphogenesis, hair growth, tooth formation, gamete formation and a wide variety of tissue and organ formation processes, and hinder the regeneration, growth, maintenance, etc., of bone and other tissues that are dependent on the BMP pathway. (I) is useful for screening for various drugs and/or antibodies that can either enhance the BMP pathway, or inhibit it by antagonizing or mimicking the **activity** of (I), respectively, and in screening assays for identifying specific ligands of (I). (I) is useful as an immunogen to generate antibodies that are useful to alter the BMP pathway by inhibiting (I) or for diagnostic purposes. (I) is useful for treating a disorder associated with BMP or TGF- beta activation, such as cancer. (I) or inhibitor of (I) can be delivered by a vector to modulate Smads, e.g. to prevent **Smurf** regulation of Smads where BMP or TGF beta **activity** is desired, such as in bone regeneration or to study **Smurf** regulator processes in vivo.

Dwg.0/18

ACCESSION NUMBER: 2001-071267 [08] WPIDS

DOC. NO. CPI: C2001-019969

TITLE: Novel isolated **Smurf** protein useful for inhibiting bone morphogenic protein or tumor growth factor-beta activation pathway, for treating cancer and to block osteogenesis, hair growth, tooth formation.

DERWENT CLASS: B04 D16

INVENTOR(S): THOMSEN, G H; WRANA, J

PATENT ASSIGNEE(S): (HSCR-N) HSC RES & DEV LP; (UYNY) UNIV NEW YORK STATE RES FOUND

COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000077168	A2	20001221	(200108)*	EN	106
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000056107	A	20010102	(200121)		
EP 1192174	A2	20020403	(200230)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003502064	W	20030121	(200308)		131
CN 1409722	A	20030409	(200345)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000077168	A2	WO 2000-US16250	20000612
AU 2000056107	A	AU 2000-56107	20000612
EP 1192174	A2	EP 2000-941398	20000612
		WO 2000-US16250	20000612
JP 2003502064	W	WO 2000-US16250	20000612
		JP 2001-504003	20000612
CN 1409722	A	CN 2000-811354	20000612

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000056107	A	Based on	WO 2000077168
EP 1192174	A2	Based on	WO 2000077168
JP 2003502064	W	Based on	WO 2000077168

PRIORITY APPLN. INFO: US 1999-138969P 19990611

L5 ANSWER 7 OF 12 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.

AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003:356072 BIOSIS
DOCUMENT NUMBER: PREV200300356072

TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads.
AUTHOR(S): Murakami, Gyo; Watabe, Tetsuro; Takaoka, Kunio; Miyazono, Kohei [Reprint Author]; Imamura, Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo, 170-8455, Japan
miyazono-ind@umin.ac.jp
SOURCE: Molecular Biology of the Cell, (July 2003) Vol. 14, No. 7, pp. 2809-2817. print.
ISSN: 1059-1524 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 6 Aug 2003

L5 ANSWER 8 OF 12 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Specificity and complexity in **Smurf**-mediated **Smad** degradation.
ACCESSION NUMBER: 2002:133151 BIOSIS
DOCUMENT NUMBER: PREV200200133151
TITLE: Specificity and complexity in **Smurf**-mediated **Smad** degradation.
AUTHOR(S): Liang, Min [Reprint author]; Lin, Xia [Reprint author]; Liang, Yao-Yun [Reprint author]; Feng, Xin-Hua [Reprint author]; DeBakey, Michael E. [Reprint author]
CORPORATE SOURCE: Department of Surgery, Baylor College of Medicine, One Baylor Plaza, 139D, Houston, TX, 77030, USA
SOURCE: Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. Supplement, pp. 148a. print.
Meeting Info.: 41st Annual Meeting of the American Society for Cell Biology. Washington DC, USA. December 08-12, 2001. American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Feb 2002
Last Updated on STN: 26 Feb 2002

L5 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
TI Impaired Smad7-**Smurf**-mediated negative regulation of TGF-β signaling in scleroderma fibroblasts
AB The principal effect of TGF-β1 on mesenchymal cells is its stimulation of ECM synthesis. Previous reports indicated the significance of the autocrine TGF-β loop in the pathogenesis of scleroderma. In this study, the authors focused on Smad7 and Smurfs, principal mols. in the neg. regulation of TGF-β signaling, to further understand the autocrine TGF-β loop in scleroderma. Scleroderma fibroblasts exhibited increased Smad7 levels compared with normal fibroblasts in vivo and in vitro. Smad7 constitutively formed a complex with the TGF-β receptors, and the inhibitory effect of Smad7 on the promoter **activity** of human α2(I) collagen and 3TP-lux was completely impaired in scleroderma fibroblasts. Furthermore, the protein stability of TGF-β receptor type I was significantly increased in scleroderma fibroblasts compared with normal fibroblasts. There was no significant difference in Smurf1 and Smurf2 levels between normal and scleroderma fibroblasts, and the transiently overexpressed Smurf1 and/or Smurf2 did not affect TGF-β receptor type I protein levels in scleroderma fibroblasts. These results indicate that the impaired Smad7-**Smurf** -mediated inhibitory effect on TGF-β signaling might contribute to maintaining the autocrine TGF-β loop in scleroderma fibroblasts. To our knowledge, this is the first report of a disturbed neg. regulation of

TGF-β signaling in fibrotic disorders.

ACCESSION NUMBER: 2004:64890 HCAPLUS
DOCUMENT NUMBER: 140:216014
TITLE: Impaired Smad7-**Smurf**-mediated negative regulation of TGF-β signaling in scleroderma fibroblasts
AUTHOR(S): Asano, Yoshihide; Ihn, Hironobu; Yamane, Kenichi; Kubo, Masahide; Tamaki, Kunihiko
CORPORATE SOURCE: Department of Dermatology, Faculty of Medicine, University of Tokyo, Tokyo, Japan
SOURCE: Journal of Clinical Investigation (2004), 113(2), 253-264
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation In addition, Smurf1 assocs. with transforming growth factor-β type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation Herein, we examined whether Smurf1 neg. regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003:571354 HCAPLUS
DOCUMENT NUMBER: 139:302479
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AUTHOR(S): Murakami, Gyo; Watabe, Tetsuro; Takaoka, Kunio; Miyazono, Kohei; Imamura, Takeshi
CORPORATE SOURCE: Department of Biochemistry, The Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo, 170-8455, Japan
SOURCE: Molecular Biology of the Cell (2003), 14(7), 2809-2817
CODEN: MBCEEV; ISSN: 1059-1524
PUBLISHER: American Society for Cell Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
TI sequences human ubiquitin-protein synthetases as antagonists of BMP and TGF<b signaling pathways and expression during development and interactions with **Smad** proteins
AB This invention provides unique members of the Hect family of ubiquitin ligases that specifically target BMP and TGF<b/activin pathway-specific Smads. The novel ligases have been named Smurf1 and Smurf2. A transgenic expression system is described for these two proteins. They directly interact with Smads1 and 5 and Smad7, resp., and regulate the

ubiquitination, turnover and **activity** of Smads and other proteins of these pathways. Smurf1 interferes with biol. responses to BMP, but not activin signaling. In amphibian embryos Smurf1 inhibits endogenous BMP signals, resulting in altered pattern formation and cell fate specification in the mesoderm and ectoderm. The present invention provides a unique regulatory link between the ubiquitination pathway and the control of cell fate determination by the TGF<b superfamily during embryonic development. Thus, Smurf1 is a neg. regulator of Smad1 signal transduction, by targeting Smad1, Smurf1 blocks BMP signaling. Screening assays which survey **Smurf** WW domain interaction with **Smad** protein PPXY domain are also relayed. In mammalian cells, Smurf2 suppresses TGF<b signaling, and in Xenopus, blocks formation of dorsal mesoderm and causes anterior truncation of the embryos. Smurf2 forms a stable complex with Smad7, which induces degradation and downregulation of TGF<b/activin signaling. The human Smurf1 gene was mapped to 7q21.1-q31.1.

ACCESSION NUMBER: 2000:900772 HCAPLUS
DOCUMENT NUMBER: 134:53133
TITLE: sequences human ubiquitin-protein synthetases as antagonists of BMP and TGF<b signaling pathways and expression during development and interactions with **Smad** proteins
INVENTOR(S): Thomsen, Gerald H.; Wrana, Jeffrey
PATENT ASSIGNEE(S): Research Foundation of State University of New York, USA; HSC Research and Development Limited Partnership
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077168	A2	20001221	WO 2000-US16250	20000612
WO 2000077168	A3	20010503		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000056107	A5	20010102	AU 2000-56107	20000612
EP 1192174	A2	20020403	EP 2000-941398	20000612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-138969P P 19990611
WO 2000-US16250 W 20000612

L5 ANSWER 12 OF 12 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AB **Smad** ubiquitin regulatory factor (**Smurf**) 1 binds to receptor-regulated Smads for bone morphogenetic proteins (BMPs) Smad1/5 and promotes their degradation. In addition, Smurf1 associates with transforming growth factor-beta type I receptor through the inhibitory **Smad** (I-**Smad**) Smad7 and induces their degradation. Herein, we examined whether Smurf1 negatively regulates BMP signaling together with the I-Smads Smad6/7. Smurf1 and Smad6 cooperatively induced

secondary axes in Xenopus embryos. Using a BMP-responsive promoter-reporter construct in mammalian cells, we found that Smurf1 cooperated with I-**Smad** in inhibiting BMP signaling and that the inhibitory **activity** of Smurf1 was not necessarily correlated with its ability to bind to Smad1/5 directly. Smurf1 bound to BMP type I receptors via I-Smads and induced ubiquitination and degradation of these receptors. Moreover, Smurf1 associated with Smad1/5 indirectly through I-Smads and induced their ubiquitination and degradation. Smurf1 thus controls BMP signaling with and without I-Smads through multiple mechanisms.

ACCESSION NUMBER: 2003:636252 SCISEARCH
THE GENUINE ARTICLE: 701CB
TITLE: Cooperative inhibition of bone morphogenetic protein signaling by Smurf1 and inhibitory Smads
AUTHOR: Murakami G; Watabe T; Takaoka K; Miyazono K (Reprint); Imamura T
CORPORATE SOURCE: Japanese Fdn Canc Res, Inst Canc, Dept Biochem, Tokyo 1708455, Japan (Reprint); Shinshu Univ, Dept Orthoped Surg, Nagano 3908621, Japan; Univ Tokyo, Dept Mol Pathol, Grad Sch Med, Tokyo 1130033, Japan; Osaka City Univ, Sch Med, Dept Orthoped Surg, Osaka 5458585, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (JUL 2003) Vol. 14, No. 7, pp. 2809-2817.
Publisher: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750, BETHESDA, MD 20814-2755 USA.
ISSN: 1059-1524.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 29
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

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Refine Search

Search Results -

Terms	Documents
L13 and L12	0

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L14

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Search History

DATE: Wednesday, September 29, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=OR			
L14	L13 and l12	0	L14
L13	wrana.in.	4	L13
L12	thomsen.in.	653	L12
L11	l7 and L10	92	L11
L10	L9 and l8	98436	L10
L9	Smurf WW domain	100821	L9
L8	PPYX domain	98436	L8
L7	l5 and L6	147	L7
L6	smad polypeptide adj ubiquitination	157	L6
L5	L4 and smad polypeptide	47417	L5
L4	L3 and smurf activity	378010	L4
L3	Smurf polypeptide	47366	L3
L2	6001619.pn.	1	L2
L1	6503742.pn.	1	L1

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END OF SEARCH HISTORY

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Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Search Results - Record(s) 1 through 4 of 4 returned.

☐ 1. Document ID: US 6727002 B2

L13: Entry 1 of 4 File: USPT Apr 27, 2004

US-PAT-NO: 6727002
DOCUMENT-IDENTIFIER: US 6727002 B2

TITLE: EVOH and EVM in single- or multilayer products

DATE-ISSUED: April 27, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hoch; Martin	Heinsberg			DE
Itter; Ulrich	Wuppertal			DE
Parg; Roland	Leverkusen			DE
Wrana; Claus	Cologne			DE
Schulte; Helmut	Krefeld			DE
Schwarz; Peter	Krefeld			DE
Ulrich; Ralph	Krefeld			DE

US-CL-CURRENT: 428/520; 264/173.19, 428/475.8, 428/476.3, 428/476.9, 428/522, 525/57

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 2. Document ID: US 6017755 A

L13: Entry 2 of 4 File: USPT Jan 25, 2000

US-PAT-NO: 6017755
DOCUMENT-IDENTIFIER: US 6017755 A

TITLE: MADR2 tumour suppressor gene

DATE-ISSUED: January 25, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wrana; Jeffrey	Toronto			CA
Attisano; Liliana	Toronto			CA

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Scherer; Stephen W. Toronto CA

US-CL-CURRENT: 435/320.1; 435/325, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 3. Document ID: US 4679483 A

L13: Entry 3 of 4 File: USPT Jul 14, 1987

US-PAT-NO: 4679483
DOCUMENT-IDENTIFIER: US 4679483 A

TITLE: Dispenser and dispensing cassette

DATE-ISSUED: July 14, 1987

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wrana; Josef B. V.	Sp.ang.nga			SE

US-CL-CURRENT: 89/1.51; 102/505, 244/137.4, 89/1.59

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 4. Document ID: US 4586439 A

L13: Entry 4 of 4 File: USPT May 6, 1986

US-PAT-NO: 4586439
DOCUMENT-IDENTIFIER: US 4586439 A

TITLE: Cartridge for launching decoys

DATE-ISSUED: May 6, 1986

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wrana; Josef B. V.	Sp.ang.nga			SE

US-CL-CURRENT: 102/438; 102/357, 102/505

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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Terms	Documents

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Previous Page Next Page Go to Doc#

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Refine Search

Search Results -

Terms	Documents
L11 and L2	0

Database:
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US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L16

Refine Search

Recall Text | Clear | Interrupt

Search History

DATE: Wednesday, September 29, 2004 Printable Copy Create Case

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L15	L11 and l1	0	L15
L14	L13 and l12	0	L14
L13	wrana.in.	4	L13
L12	thomsen.in.	653	L12
L11	l7 and L10	92	L11
L10	L9 and l8	98436	L10
L9	Smurf WW domain	100821	L9
L8	PPYX domain	98436	L8
L7	l5 and L6	147	L7
L6	smad polypeptide adj ubiquitination	157	L6
L5	L4 and smad polypeptide	47417	L5
L4	L3 and smurf activity	378010	L4
L3	Smurf polypeptide	47366	L3

h e b b cg b e e ch

L2	6001619.pn.	1	L2
L1	6503742.pn.	1	L1

END OF SEARCH HISTORY

h e b b cg b e e ch

Hit List

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Search Results - Record(s) 1 through 10 of 92 returned.

☐ 1. Document ID: US 6770626 B2

L11: Entry 1 of 92 File: USPT Aug 3, 2004

US-PAT-NO: 6770626
DOCUMENT-IDENTIFIER: US 6770626 B2

TITLE: Tissue remodeling

DATE-ISSUED: August 3, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ben-Sasson; Shmuel	Jerusalem			IL

US-CL-CURRENT: 514/15; 514/12, 514/13, 514/14, 514/16, 514/17, 530/327

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 2. Document ID: US 6770458 B1

L11: Entry 2 of 92 File: USPT Aug 3, 2004

US-PAT-NO: 6770458
DOCUMENT-IDENTIFIER: US 6770458 B1

TITLE: Purified and isolated serine-threonine kinase receptors associated protein and use of same in the modulation of the biological activity of TGF-.beta.

DATE-ISSUED: August 3, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Datta; Pran K.	Nashville	TN		
Moses; Harold L.	Nashville	TN		

US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/325, 435/70.1, 435/70.3, 435/71.1, 514/2, 536/23.1, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 3. Document ID: US 6767541 B2

L11: Entry 3 of 92 File: USPT Jul 27, 2004

US-PAT-NO: 6767541
DOCUMENT-IDENTIFIER: US 6767541 B2

TITLE: HER-2/neu overexpression abrogates growth inhibitory pathways

DATE-ISSUED: July 27, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Slamon; Dennis J.	Woodland Hills	CA		
Wilson; Cindy A.	Los Angeles	CA		
Calzone; Frank J.	Westlake Village	CA		

US-CL-CURRENT: 424/143.1; 424/130.1, 424/133.1, 424/141.1, 424/142.1, 424/152.1, 424/155.1, 424/156.1, 424/172.1, 424/174.1, 514/2, 530/387.1, 530/387.3, 530/387.7, 530/388.1, 530/388.15, 530/388.2, 530/388.22, 530/388.8, 530/388.85

Full | Title | Citation | Front | Review | Classification | Date | Reference | [illegible] | Claims | KWMC | Draw De

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☐ 4. Document ID: US 6764677 B1

L11: Entry 4 of 92 File: USPT Jul 20, 2004

US-PAT-NO: 6764677
DOCUMENT-IDENTIFIER: US 6764677 B1

TITLE: Tango 294, a lipase-like protein

DATE-ISSUED: July 20, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sharp; John D.	Arlington	MA		
Barnes; Thomas M.	Brookline	MA		

US-CL-CURRENT: 424/94.1; 435/69.1, 435/69.7, 514/2, 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | [illegible] | Claims | KWMC | Draw De

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☐ 5. Document ID: US 6756215 B1

L11: Entry 5 of 92 File: USPT Jun 29, 2004

US-PAT-NO: 6756215
DOCUMENT-IDENTIFIER: US 6756215 B1

TITLE: Functionalized TGF-.beta. fusion proteins

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DATE-ISSUED: June 29, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wolfraim; Lawrence A.	Silver Spring	MD		
Letterio; John J.	Bethesda	MD		

US-CL-CURRENT: 435/69.1; 435/252.3, 435/254.2, 435/325, 435/69.7, 530/300, 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 6. Document ID: US 6747128 B2

L11: Entry 6 of 92 File: USPT Jun 8, 2004

US-PAT-NO: 6747128
DOCUMENT-IDENTIFIER: US 6747128 B2

TITLE: Components of ubiquitin ligase complexes, and uses related thereto

DATE-ISSUED: June 8, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Caligiuri; Maureen	Reading	MA		
Rolfe; Mark	Newton	MA		

US-CL-CURRENT: 530/350; 435/183, 435/219, 435/252.3, 435/254.11, 435/320.1, 435/325, 536/23.1, 536/23.2, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 7. Document ID: US 6747005 B1

L11: Entry 7 of 92 File: USPT Jun 8, 2004

US-PAT-NO: 6747005
DOCUMENT-IDENTIFIER: US 6747005 B1

TITLE: Assays, methods and means for modulating nuclear localization

DATE-ISSUED: June 8, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kouzarides; Tony	Cambridge			GB

US-CL-CURRENT: 514/12; 435/15, 435/6, 435/69.1, 435/7.1, 514/2, 530/300, 530/350, 536/23.1

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Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

☐ 8. Document ID: US 6720181 B1

L11: Entry 8 of 92 File: USPT Apr 13, 2004

US-PAT-NO: 6720181
DOCUMENT-IDENTIFIER: US 6720181 B1

TITLE: Ubiquitin ligases as therapeutic targets

DATE-ISSUED: April 13, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Chiaur; Dah Shiarn	New York	NY		
Pagano; Michele	New York	NY		
Latres; Esther	New York	NY		

US-CL-CURRENT: 435/325; 435/320.1, 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

☐ 9. Document ID: US 6716597 B2

L11: Entry 9 of 92 File: USPT Apr 6, 2004

US-PAT-NO: 6716597
DOCUMENT-IDENTIFIER: US 6716597 B2

TITLE: Methods and products for regulating cell motility

DATE-ISSUED: April 6, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gertler; Frank B.	Boston	MA		
Bear; James E.	Brighton	MA		
Loureiro; ,Joseph J.	Cambridge	MA		
Wehland; Jurgen	Bad Harzburg			DE

US-CL-CURRENT: 435/29

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

☐ 10. Document ID: US 6716589 B2

L11: Entry 10 of 92 File: USPT Apr 6, 2004

h e b b g e e e f e f g ef b e

US-PAT-NO: 6716589
DOCUMENT-IDENTIFIER: US 6716589 B2

TITLE: Discordant helix stabilization for prevention of amyloid formation

DATE-ISSUED: April 6, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Johansson; Jan	Stockholm			SE

US-CL-CURRENT: 435/7.2

Terms	Documents
L7 and L10	92

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Hit List

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Search Results - Record(s) 11 through 20 of 92 returned.

☐ 11. Document ID: US 6713616 B2

L11: Entry 11 of 92 File: USPT Mar 30, 2004

US-PAT-NO: 6713616
DOCUMENT-IDENTIFIER: US 6713616 B2

TITLE: High affinity TGF.beta. nucleic acid ligands and inhibitors

DATE-ISSUED: March 30, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pagratis; Nikos	Boulder	CO		
Lochrie; Michael	Louisville	CO		
Gold; Larry	Boulder	CO		

US-CL-CURRENT: 536/23.1; 536/25.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

☐ 12. Document ID: US 6713267 B2

L11: Entry 12 of 92 File: USPT Mar 30, 2004

US-PAT-NO: 6713267
DOCUMENT-IDENTIFIER: US 6713267 B2

TITLE: Biochemical assay to monitor the ubiquitin ligase activities of cullins

DATE-ISSUED: March 30, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Deshaies; Raymond J.	Claremont	CA		
Feldman; R. M. Renny	San Marino	CA		

US-CL-CURRENT: 435/7.1; 435/325, 435/4, 435/6, 435/7.2, 435/7.21, 436/501, 530/300, 530/350, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 13. Document ID: US 6706867 B1

L11: Entry 13 of 92 File: USPT Mar 16, 2004

US-PAT-NO: 6706867
DOCUMENT-IDENTIFIER: US 6706867 B1

TITLE: DNA array sequence selection

DATE-ISSUED: March 16, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lorenz; Matthias	Bethesda	MD		

US-CL-CURRENT: 536/23.1; 435/6, 536/24.3, 536/24.31, 536/24.32

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

☐ 14. Document ID: US 6696260 B1

L11: Entry 14 of 92 File: USPT Feb 24, 2004

US-PAT-NO: 6696260
DOCUMENT-IDENTIFIER: US 6696260 B1

TITLE: Methods to identify growth differentiation factor (GDF) binding proteins

DATE-ISSUED: February 24, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lee; Se-Jin	Baltimore	MD		
McPherron; Alexandra	Baltimore	MD		

US-CL-CURRENT: 435/7.21; 435/320.1, 435/325, 435/69.1, 435/7.1, 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

☐ 15. Document ID: US 6696256 B1

L11: Entry 15 of 92 File: USPT Feb 24, 2004

US-PAT-NO: 6696256
DOCUMENT-IDENTIFIER: US 6696256 B1
**** See image for Certificate of Correction ****

TITLE: Method, array and kit for detecting activated transcription factors by hybridization array

h e b b cg b cc e

DATE-ISSUED: February 24, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Li; Xianqiang	Palo Alto	CA		

US-CL-CURRENT: 435/7.1; 435/4, 435/6, 435/DIG.2, 530/300, 536/22.1, 536/23.1, 536/23.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 16. Document ID: US 6692925 B1

L11: Entry 16 of 92 File: USPT Feb 17, 2004

US-PAT-NO: 6692925
DOCUMENT-IDENTIFIER: US 6692925 B1

TITLE: Proteins having serine/threonine kinase domains, corresponding nucleic acid molecules, and their use

DATE-ISSUED: February 17, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Miyazono; Kohei	Shiki			JP
Imamura; Takeshe	Tokyo			JP
Dijke; Peter ten	Amsterdam			NL

US-CL-CURRENT: 435/7.2; 435/325, 435/69.1, 435/69.7, 435/7.21, 530/350, 530/387.1, 530/388.22, 530/388.23, 530/389.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 17. Document ID: US 6692744 B2

L11: Entry 17 of 92 File: USPT Feb 17, 2004

US-PAT-NO: 6692744
DOCUMENT-IDENTIFIER: US 6692744 B2
**** See image for Certificate of Correction ****

TITLE: Betaglycan as an inhibin receptor and uses thereof

DATE-ISSUED: February 17, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Vale; Wylie	La Jolla	CA		
Lewis; Kathy A.	San Diego	CA		

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Gray; Peter C.	Encinitas	CA
Bilezikjian; Louise M.	San Diego	CA
Blount; Amy L.	La Jolla	CA

US-CL-CURRENT: 424/158.1; 530/350, 530/387.9, 530/388.1, 530/389.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 18. Document ID: US 6673596 B1

L11: Entry 18 of 92 File: USPT Jan 6, 2004

US-PAT-NO: 6673596
DOCUMENT-IDENTIFIER: US 6673596 B1

TITLE: In vivo biosensor apparatus and method of use

DATE-ISSUED: January 6, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sayler; Gary S.	Blain	TN		
Simpson; Michael L.	Knoxville	TN		
Applegate; Bruce M.	Knoxville	TN		
Ripp; Steven A.	Knoxville	TN		

US-CL-CURRENT: 435/288.7; 422/55, 422/58, 422/61, 422/82.05, 435/288.2, 435/288.5, 435/7.1, 435/8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 19. Document ID: US 6673570 B1

L11: Entry 19 of 92 File: USPT Jan 6, 2004

US-PAT-NO: 6673570
DOCUMENT-IDENTIFIER: US 6673570 B1

TITLE: Smad associating polypeptides

DATE-ISSUED: January 6, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Itoh; Fumiko	Uppsala			SE
Itoh; Susumu	Uppsala			SE
Heldin; Carl-Henrik	Uppsala			SE
Dijke; Peter ten	Amsterdam			NL

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US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/325, 530/350, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | [illegible] | Claims | KWMC | Draw De

☐ 20. Document ID: US 6673352 B1

L11: Entry 20 of 92 File: USPT Jan 6, 2004

US-PAT-NO: 6673352
DOCUMENT-IDENTIFIER: US 6673352 B1

TITLE: Use of Mullerian inhibiting substance for treating excess androgen states

DATE-ISSUED: January 6, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Donahoe; Patricia K.	Boston	MA		
Teixeira; Jose	Boston	MA		
Fynn-Thompson; Eric	Boston	MA		

US-CL-CURRENT: 424/198.1; 435/7.21, 514/2, 530/324, 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | [illegible] | Claims | KWMC | Draw De

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Terms	Documents
L7 and L10	92

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Previous Page Next Page Go to Doc#

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☐ 1. Document ID: US 6770626 B2

L7: Entry 1 of 147 File: USPT Aug 3, 2004

US-PAT-NO: 6770626
DOCUMENT-IDENTIFIER: US 6770626 B2

TITLE: Tissue remodeling

DATE-ISSUED: August 3, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ben-Sasson; Shmuel	Jerusalem			IL

US-CL-CURRENT: 514/15; 514/12, 514/13, 514/14, 514/16, 514/17, 530/327

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 2. Document ID: US 6770458 B1

L7: Entry 2 of 147 File: USPT Aug 3, 2004

US-PAT-NO: 6770458
DOCUMENT-IDENTIFIER: US 6770458 B1

TITLE: Purified and isolated serine-threonine kinase receptors associated protein and use of same in the modulation of the biological activity of TGF-.beta.

DATE-ISSUED: August 3, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Datta; Pran K.	Nashville	TN		
Moses; Harold L.	Nashville	TN		

US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/325, 435/70.1, 435/70.3, 435/71.1, 514/2, 536/23.1, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 3. Document ID: US 6767541 B2

L7: Entry 3 of 147 File: USPT Jul 27, 2004

US-PAT-NO: 6767541
DOCUMENT-IDENTIFIER: US 6767541 B2

TITLE: HER-2/neu overexpression abrogates growth inhibitory pathways

DATE-ISSUED: July 27, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Slamon; Dennis J.	Woodland Hills	CA		
Wilson; Cindy A.	Los Angeles	CA		
Calzone; Frank J.	Westlake Village	CA		

US-CL-CURRENT: 424/143.1; 424/130.1, 424/133.1, 424/141.1, 424/142.1, 424/152.1, 424/155.1, 424/156.1, 424/172.1, 424/174.1, 514/2, 530/387.1, 530/387.3, 530/387.7, 530/388.1, 530/388.15, 530/388.2, 530/388.22, 530/388.8, 530/388.85

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 4. Document ID: US 6765002 B2

L7: Entry 4 of 147 File: USPT Jul 20, 2004

US-PAT-NO: 6765002
DOCUMENT-IDENTIFIER: US 6765002 B2

TITLE: Prevention of ovarian cancer by administration of products that induce transforming growth factor-.beta. and/or apoptosis in the ovarian epithelium

DATE-ISSUED: July 20, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rodriguez; Gustavo C.	Durhman	NC		

US-CL-CURRENT: 514/177

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 5. Document ID: US 6764677 B1

L7: Entry 5 of 147 File: USPT Jul 20, 2004

US-PAT-NO: 6764677
DOCUMENT-IDENTIFIER: US 6764677 B1

TITLE: Tango 294, a lipase-like protein

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DATE-ISSUED: July 20, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sharp; John D.	Arlington	MA		
Barnes; Thomas M.	Brookline	MA		

US-CL-CURRENT: 424/94.1; 435/69.1, 435/69.7, 514/2, 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 6. Document ID: US 6756215 B1

L7: Entry 6 of 147 File: USPT Jun 29, 2004

US-PAT-NO: 6756215
DOCUMENT-IDENTIFIER: US 6756215 B1

TITLE: Functionalized TGF-.beta. fusion proteins

DATE-ISSUED: June 29, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wolfraim; Lawrence A.	Silver Spring	MD		
Letterio; John J.	Bethesda	MD		

US-CL-CURRENT: 435/69.1; 435/252.3, 435/254.2, 435/325, 435/69.7, 530/300, 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 7. Document ID: US 6747128 B2

L7: Entry 7 of 147 File: USPT Jun 8, 2004

US-PAT-NO: 6747128
DOCUMENT-IDENTIFIER: US 6747128 B2

TITLE: Components of ubiquitin ligase complexes, and uses related thereto

DATE-ISSUED: June 8, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Caligiuri; Maureen	Reading	MA		
Rolfe; Mark	Newton	MA		

US-CL-CURRENT: 530/350; 435/183, 435/219, 435/252.3, 435/254.11, 435/320.1, 435/325, 536/23.1, 536/23.2, 536/23.5

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Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 8. Document ID: US 6747005 B1

L7: Entry 8 of 147 File: USPT Jun 8, 2004

US-PAT-NO: 6747005
DOCUMENT-IDENTIFIER: US 6747005 B1

TITLE: Assays, methods and means for modulating nuclear localization

DATE-ISSUED: June 8, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kouzarides; Tony	Cambridge			GB

US-CL-CURRENT: 514/12; 435/15, 435/6, 435/69.1, 435/7.1, 514/2, 530/300, 530/350, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 9. Document ID: US 6720181 B1

L7: Entry 9 of 147 File: USPT Apr 13, 2004

US-PAT-NO: 6720181
DOCUMENT-IDENTIFIER: US 6720181 B1

TITLE: Ubiquitin ligases as therapeutic targets

DATE-ISSUED: April 13, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Chiaur; Dah Shiarn	New York	NY		
Pagano; Michele	New York	NY		
Latres; Esther	New York	NY		

US-CL-CURRENT: 435/325; 435/320.1, 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 10. Document ID: US 6716597 B2

L7: Entry 10 of 147 File: USPT Apr 6, 2004

US-PAT-NO: 6716597
DOCUMENT-IDENTIFIER: US 6716597 B2

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TITLE: Methods and products for regulating cell motility

DATE-ISSUED: April 6, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gertler; Frank B.	Boston	MA		
Bear; James E.	Brighton	MA		
Loureiro; Joseph J.	Cambridge	MA		
Wehland; Jurgen	Bad Harzburg			DE

US-CL-CURRENT: 435/29

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L11	l7 and L10	92	L11
L10	L9 and l8	98436	L10
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L8	PPYX domain	98436	L8
L7	l5 and L6	147	L7
L6	smad polypeptide adj ubiquitination	157	L6
L5	L4 and smad polypeptide	47417	L5
L4	L3 and smurf activity	378010	L4
L3	Smurf polypeptide	47366	L3

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